POST-INTUBATION LARYNGEAL INJURIES IN A PAEDIATRIC INTENSIVE CARE UNIT OF TERTIARY HOSPITAL IN INDIA:

A FIBREOPTIC ENDOSCOPIC STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF

M.S BRANCH –IV (OTORHINOLARYNGOLOGY)

EXAMINATION OF THE TAMILNADU DR.MGR. MEDICAL UNIVERSITY, TO BE HELD IN **MARCH 2013**

CERTIFICATE

This is to certify that the dissertation entitled **'Post-intubation laryngeal injuries in a paediatric intensive care unit of tertiary hospital in India: A fibreoptic endoscopic study'** is a bonafide original work of **Dr Bhartendu Bharti,** submitted in partial fulfilment of the rules and regulations for the MS Branch IV, Otorhinolaryngology examination of The Tamil Nadu Dr. M.G.R Medical University to be held in April 2012.

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And to God be the glory, great things He hath done.

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INTRODUCTION

In current medical practice, critical care technology and assisted ventilation have grown immensely over the past few decades. Critically ill patients are treated with prolonged assisted ventilation. Intubation is a routine procedure in such patients, and it might take several weeks either to extubate or tracheotomise these patients. Laryngotracheal intubation in adults was first done around 1878 by a British surgeon, William McEwen, who used a brass fashioned tube for orotracheal intubation. [1] By 1910's, O'Dwyer, Elsborg, and several others contributed to making it acceptable for induction of anaesthesia. [2, 3] It was Bergstorm who first provided prolonged intubation for comatose patients due to head injury or poisoning in 1962. [4] Paediatric intubations, however, were considered unsafe and were not in practice till the 1930's. Subsequent advancements in anaesthesiology in the 1940's made paediatric intubation more acceptable. [5]

Lindholm, in 1969, first reported intubation to be responsible for injuries to the larynx and trachea, and suggested that the size and shape of the tube might contribute to the problems in the posterior glottis. [6] Intubation and assisted ventilation can cause temporary or permanent damage to the airway. Inappropriate sized tube and traumatic intubation are considered the most common causes of laryngeal injury.

Direct laryngoscopy was the method of choice to assess these injuries till the development of flexible laryngobronchoscopes. Robert Wood and colleagues first studied the airway of infants and children with the help of fibreoptic scope after which it became the method of choice. [7] The advantage of a small diameter flexible scope is that it allows the study the larynx in patients who are awake, thus avoiding general anaesthesia. Moreover, it gives valuable information about vocal fold mobility or prolapse in the laryngopharynx.

With the advent of disposable and 'High volume-Low pressure' endotracheal tubes in 1970, the occurrence of reactive injuries and infection have significantly decreased, due to which ICU survival rates increased dramatically. As a result, laryngeal injuries are often overlooked, and potentially complicate treatment of these patients. [8, 9]

Several studies had been done in adults to evaluate acute post-laryngeal injuries and associated factors for post extubation stridor (PES). However, very few studies have been done in the paediatric age group. Hence, this study was conducted in the paediatric age group with the help of flexible laryngoscope. Our goal was to identify the patients who were at risk for laryngeal injury after prolonged intubation.

AIMS AND OBJECTIVES

To identify acute laryngeal injuries in paediatric patients intubated for more than 48 hours

To correlate these injuries with age of child, size and type of tube, skill level of the intubator and duration of intubation

REVIEW OF LITERATURE

DEVELOPMENTAL ANATOMY:

The larynx, trachea, bronchi and lungs develop at 4^{th} week of gestation, from a midline ventral respiratory diverticulum of the foregut known as laryngotracheal groove situated posterior to the hypobranchial eminence. The endodermal lining of this diverticulum gives rise to the epithelium of the lower respiratory tract. The diverticulum elongates in the caudal direction and is separated from the foregut by the esophagotracheal septum and eventually the tube separates from the esophagus in caudo-cranial direction except at the cranial most end. This opening represents the primitive aditus to the larynx. The caudal end of the tube becomes bilobed, known as the right and left lung buds. In the upper end of the fused ridges, two swellings appear, arytenoid swellings, with a small cleft in between. The cleft usually remains occluded till the third month of intra-uterine life. The epiglottis develops from the posterior part of hypobranchial eminence and is connected to the arytenoid swelling on either side by the aryepiglottic fold. The aryepiglottic folds deepens, primitive aditus now becomes the glottis. The laryngeal cartilages develop during the second month of intrauterine life. They appear in the branchial mesoderm where it surrounds the upper part of the respiratory diverticulum. (Figure- 1, 2, 3).The thyroid and cuneiform cartilages develop from fourth arch, cricoid, corniculate and arytenoids develop from sixth arch.[10, 11, 12]

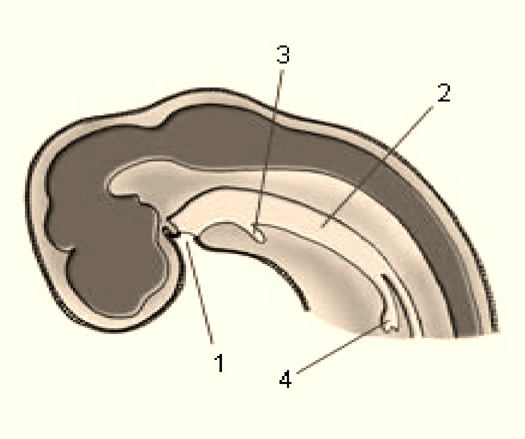

Fig 1:

1. Stomodeum
2. Pharyngeal gut
3. Thyroglossal duct
4. Tracheobronchial diverticulum

From Atlas of human embryology chronolab

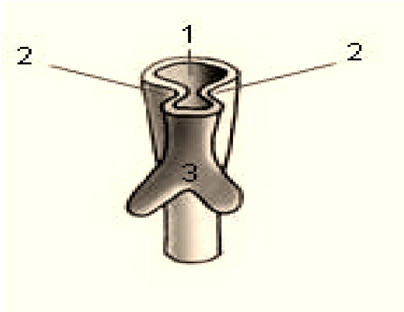

Fig 2:

1. Foregut
2. Esophagotracheal septum
3 . Respiratory diverticulum

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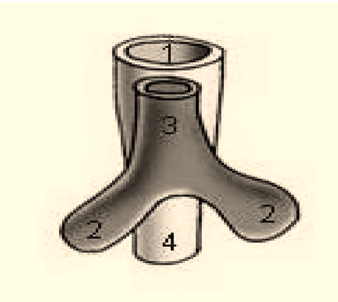


Fig 3:

1. Pharynx
2. Lung buds
3. Trachea
4. Esophagus

From Atlas of human embryology chronolab

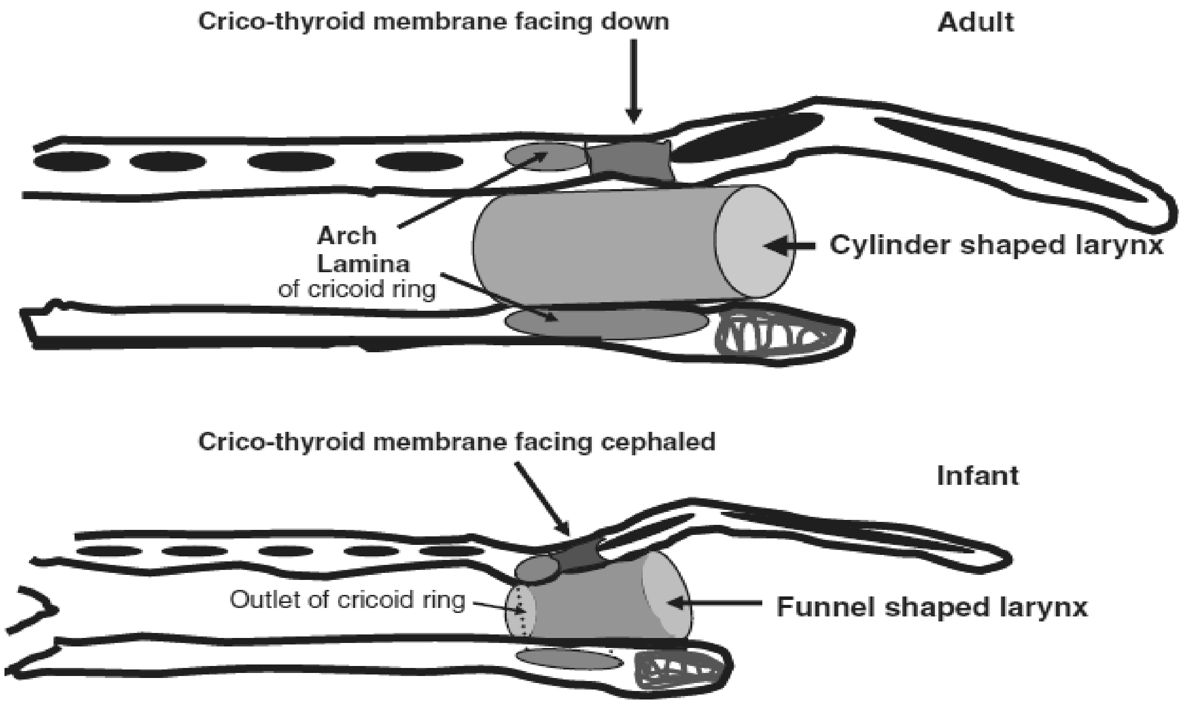
INFANT LARYNX:

The infant larynx is shorter and stouter than the adult larynx. At birth the infant larynx is approximately one third the size of adult larynx and is situated higher in the cervical region. The inferior margin of the cricoid cartilage is at the level of fourth cervical vertebra (C4), and the tip of epiglottis is at the level of first cervical vertebrae (C1). The epiglottis and soft palate are in close approximation to each other. This permits suckling and simultaneous respiration in the newborn and also contributes to baby's obligate nasal breathing.

The thyroid cartilage is within the arch of hyoid and slightly inferior to it. The vocal cords are oriented transversely in the newborn, the epiglottis is short, and the aryepiglottic folds are thick and bulky. The arytenoids are comparatively large and are expanded by a thick areolar submucosa.

The dimensions of newborn glottis are 7mm and 4mm anterio-posteriorly and laterally respectively. The narrowest portion is subglottis with a diameter of 4 – 5 mm. The mucus producing glands are abundantly present in thick submucosa in subglottis. These mucus producing glands can be injured during intubation giving rise to acquired subglottic cysts. (Figure: 4) [13]

Figure: 4[13] Difference between infant and adult larynx. From: Josef Holzki. Paediatric anaesthesia, 2009



PAEDIATRIC LARYNX:

The position, structure, and function of the larynx continue to evolve throughout childhood. Larynx gradually descends in the neck to reach the level of fifth cervical vertebra (C5) by the age of 2 years, sixth cervical vertebra (C6) by 5 years of age and finally sixth to seventh cervical vertebra (C6-7) by 15 years. The thyroid cartilage and hyoid bone, which overlap in the newborn, separate during laryngeal descent.

Larynx of the child grows very rapidly from birth till the age of 3 years after which it slows down till puberty. All the structures of larynx grows in proportion with each other till puberty, except the epiglottis which grows vertically faster than rest of the larynx and also increases in curvature to attain adult configuration. The relative position of vocal folds with thyroid cartilage remains same. Cricoid cartilage maintains 30 degrees angle with the true vocal cords, and the arytenoids are one third the anterior height of the thyroid cartilage. [14]

Larynx undergoes remarkable changes in the second decade of life. Thyroid cartilage grows in size and produces thyroid prominence. Arytenoids grow slowly compared to rest of larynx. The ratio between membranous and cartilaginous parts of vocal fold in neonate is approximately 50%, which is more suitable for respiratory function while during adolescence under the influence of hormonal growth spurt membranous part increases significantly to occupy six tenths of total length of the cord. This high ratio between membranous and cartilaginous part serves the phonatory function much better. The anterioposterior diameter of the glottis increases as well as thyroid cartilage angle becomes more acute from 120 degrees to 90 degrees in both sexes. Vocal cord grows twice as fast in length in male as compared to a female. [15, 16]

By the time larynx size reaches the adult size it undergoes significant changes in anatomical structures like position which is now placed lower down at the level of 3rd -6th cervical vertebra , shape of epiglottis which is now more leaf like rather than floppy omega shaped epiglottis in infants, cartilages becomes more rigid. Narrowest area in infants changes from subglottis to glottis in adults where submucosal tissue is more abundant and loose in comparison to adults. These features make infant and children more prone getting airway obstruction even with minor trauma or inflammation.

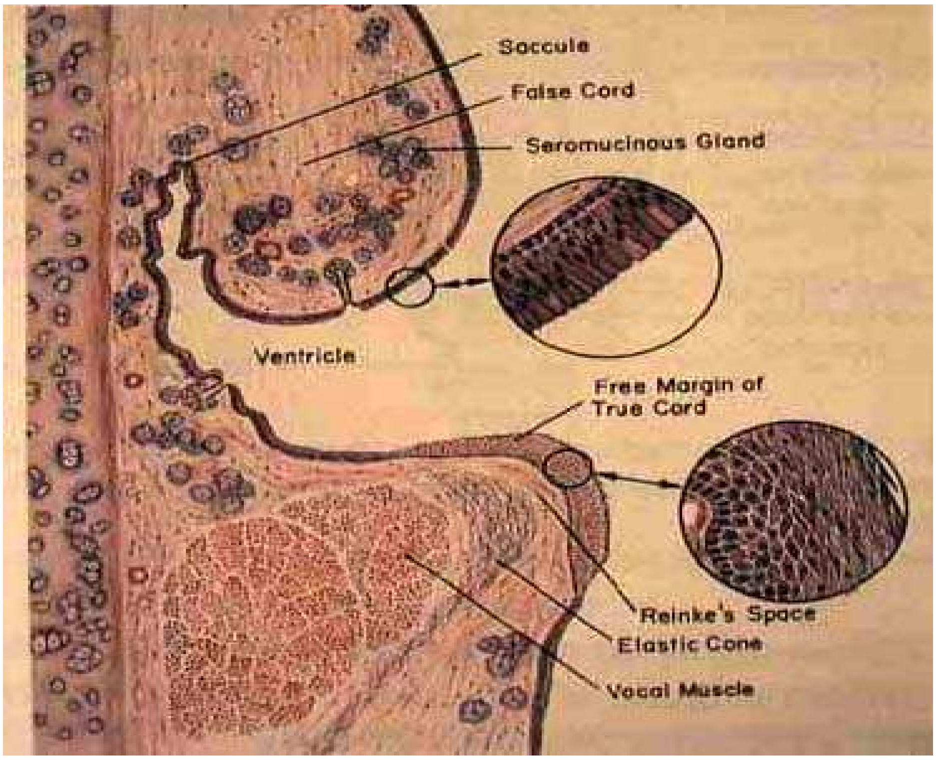
Table 1: Difference between infant and adult larynx

	Infant Larynx	**Adult Larynx**
Position	Superiorly placed	3^{rd} -6^{th} cervical vertebrae
Epiglottis	Omega shaped, floppy	Leaf-like
Cartilages	Soft	Rigid
Narrowest area	Subglottis	Glottis
Submucosal tissue	More abundant	Less
Adam’s apple	Less prominent	Prominent

EPITHELIUM:

Mucus membrane lining the larynx is continuous with the pharynx above and the trachea below. It is loosely attached to the walls, except over the posterior surface of the epiglottis, over the corniculate and cuneiform cartilages, and over the vocal ligaments, where it is firmly adherent to the underlying structures. The epithelium of the larynx is of three types. The entire larynx is lined by respiratory epithelium, pseudo stratified columnar ciliated epithelium except in few areas. The upper half of the posterior surface of epiglottis, upper part of aryepiglottic fold, true vocal cords, posterior commissure are lined by non-keratinizing stratified squamous epithelium. Transitional epithelium is found 4-5 mm from the free margin on the superior surface of true vocal cords and in the subglottis where the epithelium changes from squamous to respiratory type. Mucus glands are freely distributed throughout and are particularly numerous on the posterior surface of the epiglottis, lower part of the aryepiglottic folds, and in the saccule. The true vocal cords do not possess any glands, and are lubricated from those present within the saccule. (Figure: 5) [17]

Figure: **5** cross section of vocal fold



Cross section through larynx showing vocal folds lined by mucous membrane.

PATHOGENESIS OF INJURIES:

When pressure exerted by endotracheal tube exceeds the capillary pressure in the mucosa, microcirculation in the mucosa and mucoperichondrium gets compromised leading to ischemia and necrosis. Oedema, hyperaemia, ulceration and granulation set in chronological order. Most common site for injury in adults is posterior glottis while in case of infants and children subglottis is the most affected area. The possibility that different types of laryngeal injuries could be responsible for post extubation stridor (PES) requiring reintubation does not seem negligible. Post intubation laryngeal and tracheal stenosis has also been reported. [18]

Endotracheal tube which lies in posterior glottis, affects the medial surface and vocal process of arytenoid cartilage, crico-arytenoid joint, interarytenoid region and cricoid cartilage below. (Figure 6, 7).[1] Some individual are able to tolerate the pressure exerted by the endotracheal tube to a greater extent while others develops significant injuries even after intubation for few hours. This individual variability in susceptibility to develop injury is still an enigma. Several factors might contribute to the development of laryngeal injuries like laryngopharyngeal reflux, infection, hypotension etc. Another mechanism of injury to the mucosa can be the weight of the respirator tube which when unsupported, tugs on the endotracheal tube. This can cause a shearing strain on the laryngo-tracheal mucosa. [19, 20, 21]

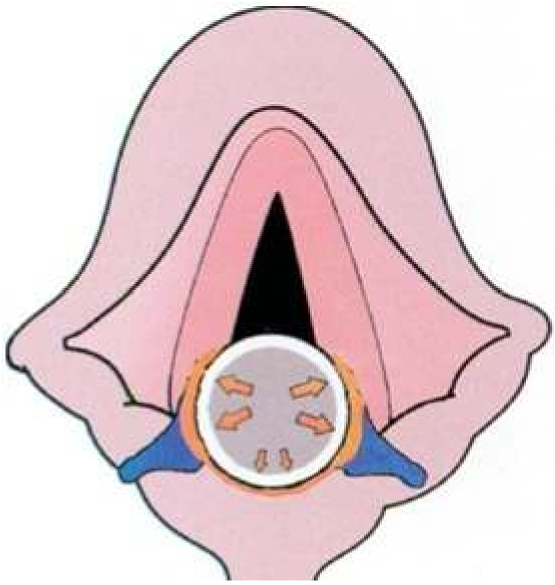


Figure 6:[1] Endotracheal tube lying in posterior glottis, exerting pressure on surrounding structure. From: Benjamin and Hollinger. Ann otorhinolaryngol 2008

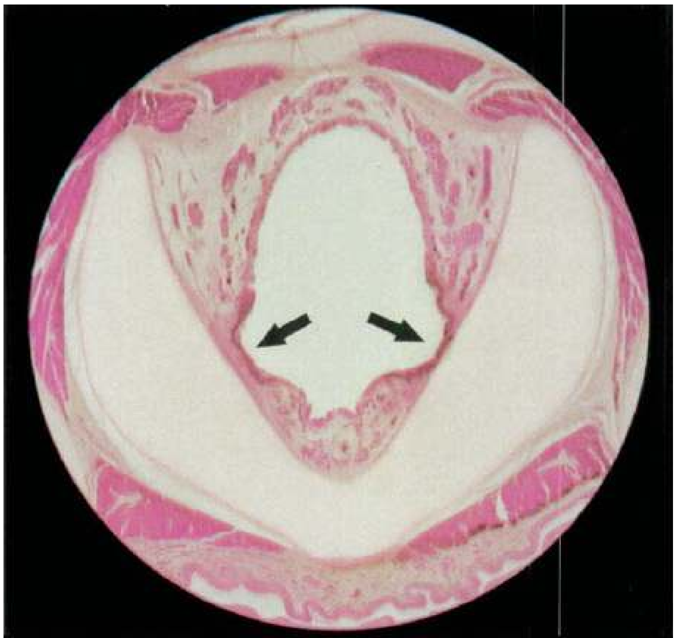


Figure 7: [1] Section through upper subglottic larynx, showing V-shape of cricoid cartilage with shallow ulcers (arrows) due to pressure necrosis via endotracheal tube. From: Benjamin and Hollinger. Ann otorhinolaryngol 2008

Initially within few hours of intubation superficial ulceration may be seen. These ulcerations heal without scarring on removal of endotracheal tube. Continuous pressure due to presence of tube, however, leads to progressive vascular damage, hyper permeability, and migration of inflammatory cells causing erosions. Small erosions usually heal by regeneration and re-epitheliazation. If healing is incomplete squamous epithelium replaces normal epithelium. [22]

If endotracheal tube is kept for longer periods, the tube acts like a foreign body. The inflammatory process around the tube may progress to ulceration and necrosis of mucosa and mucoperichondrium. This further causes perichondritis and destructive chondritis. Factors like super infection with bacteria and reflux may potentiate this process. Development of cartilage necrosis leads to weakening and collapse of cartilage causing distortion in cartilaginous framework. [23]

Accumulation of lymphocytes and macrophages takes place at the margin and base of erosion or ulcer in chronic phase of inflammation. Later fibroblasts become active in healing leading to scar tissue formation. In next few weeks or months remodelling and contraction of wound occurs during which inflammatory cells decreases, capillaries are resorbed and there is formation of collagen from fibrocytes.[24]

The shape of cricoid cartilage is different at different levels in infants and younger children. It is 'V' shaped superiorly, elliptical in middle while round shaped inferiorly. Hence pressure changes are likely to be seen in midline posteriorly. With advancement of age subglottis assumes circular shape where pressure changes are more symmetric.[1]

PATHOPHYSIOLOGY

Oedema and hyperaemia are the first changes seen on laryngeal mucosa on irritation by endotracheal tube. It mainly affects three regions i) Reinke's space over the vocal cords, ii) over the ventricular mucosa and iii) in the subglottis. (Figure: 8) Supraglottic and glottis oedema is usually mild and resolves spontaneously after removal of endotracheal tube, rarely causing any significant morbidity. But subglottic oedema often causes airway obstruction especially in paediatric age group. Endotracheal tube serves as a stent in subglottis but once it is removed the swollen mucosa becomes more prominent causing significant airway obstruction, sometimes requiring reintubation. [25, 26] Oedema within the submucosa in the subglottis at the level of the cricoid may increase slowly leading to delayed airway obstruction, hours after the removal of the endotracheal tube.

Ulceration with varying degrees of granulation tissue formation is not unusual due to prolonged contact with the tube, with posterior larynx being the most susceptible owing to its 'V' shape. This granulation tissue formation begins within 48 hours. Benjamin describes "tongues of granulation" extending from the vocal processes bilaterally anterior to the endotracheal tube, when large enough can prolapse into the glottis at extubation causing airway obstruction which may require immediate re-intubation. (Figure: 9, 10) According to Benjamin removal of granulation tissue is unnecessary as it will likely resolve but Deeb et al suggested to remove the granulation obscuring the airway at the time of tracheostomy itself in failed extubation cases to prevent long term complications. [27, 28, 29]

Figure 8 [1]:

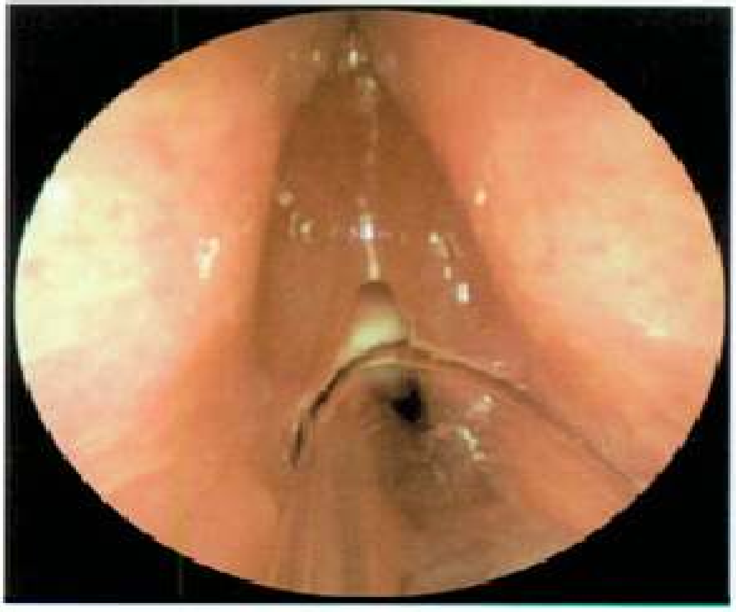


Figure 8- Vocal fold Oedema with endotracheal tube lying in posterior glottis. From: Benjamin and Hollinger. Ann otorhinolaryngol 2008

Figure 9[1]:

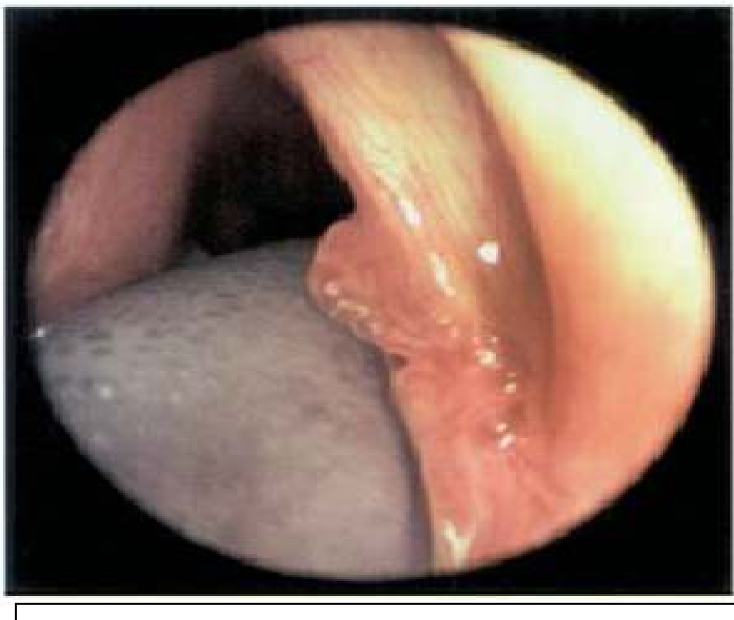


Figure 9- Vocal fold granulations on at the site of contact with the endotracheal tube. From: Benjamin and Hollinger. Ann otorhinolaryngol 2008

Figure 10[1]:

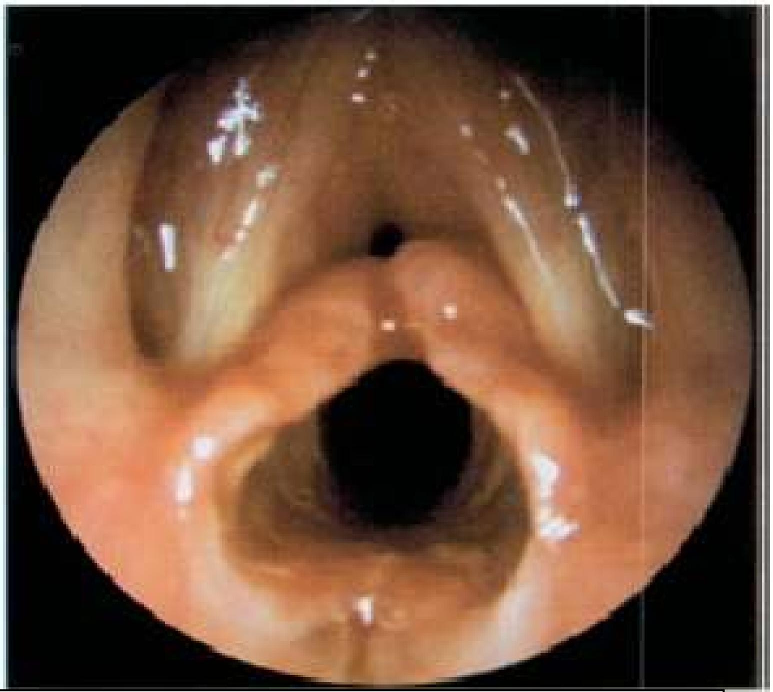


Figure 10 – Tongues of granulation tissue. From: Benjamin and Hollinger. Ann otorhinolaryngol 2008

In some instances, the granulation tissue resolves incompletely or can mature into chronic laryngeal scarring. With incomplete healing and persistent perichondritis, an intubation granuloma may form. This is a localized, rounded mass that protrudes from the site of ulceration, most commonly at the vocal process and medial surface of the arytenoid. At laryngoscopy it is noted as a globular, yellow-red pedunculated mass. Granulomas arising in other sites are often the result of a mucosal laceration. Patients with intubation granuloma present weeks to months after extubation with voice changes, globus or rarely with symptoms of airway obstruction. Injury at the free edge of the vocal fold heals with scarring. These lesions occur most commonly near the vocal process of the arytenoid. This may mature into a healed fibrous nodule covered with intact mucosa. [1, 13] Once the endotracheal tube is removed, large tongues of granulation tissue may fall towards the midline contacting one another. Adherence and healing in this configuration may result in formation of a bridge of scar tissue, an interarytenoid adhesion. The vocal folds may be tethered to one another, limiting abduction and mimicking vocal fold paralysis. Deep ulceration commonly occurs with chondritis of the arytenoid and cricoid cartilages. After intubation, these ulcerations heal with marked scarring. In severe cases, this scarring matures into a thick fibrous band between the arytenoid cartilages. (Figure: 11, 12) [1, 13] This results in restricted abduction of true vocal cords which can be incorrectly interpreted as bilateral abductor paralysis. This paralysis without the nerve involvement can be named as pseudo laryngeal paralysis.

Figure 11[13]:

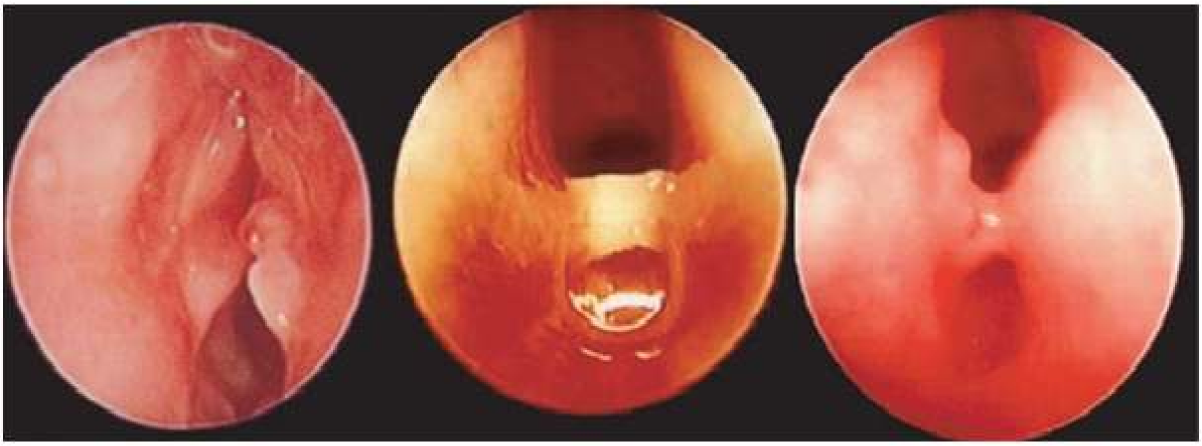


Figure 11 – Formation of granulations, adhesions and synechiae in the posterior glottis. From: Josef Holzki. Paediatric anaesthesia 2009.

Figure 12[1] :

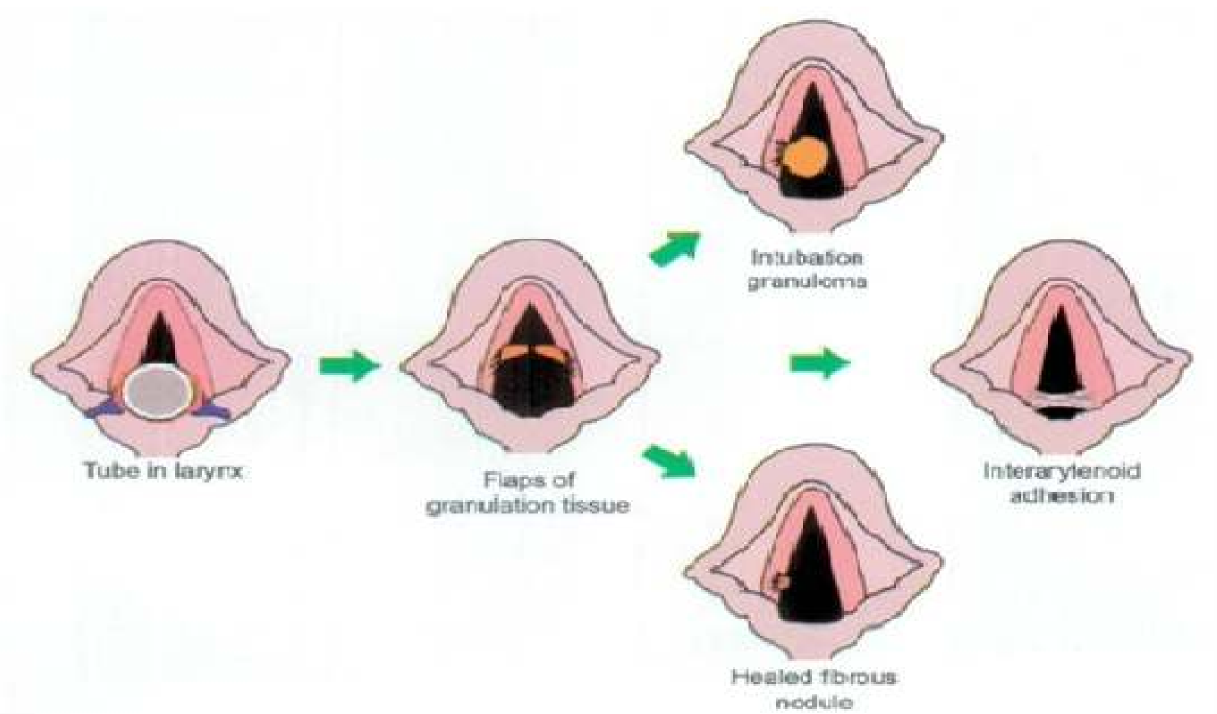


Figure 12 – Diagrammatic representation of vocal fold injury sequelae. From: Benjamin and Hollinger. Ann otorhinolaryngol 2008

As mentioned previously, posterior glottis is the site most susceptible to injury from prolonged intubation. Pressure necrosis and ulceration occur over the medial surface of the arytenoid and within the cricoid. Superficial ulceration may start as early as 4-6 hours after intubation. As the irritation from the endotracheal tube persists, the mucosal ulcerations deepen and are invaded by bacteria from the respiratory tree. The inflammatory reaction reaches the perichondrium in about two days . Prolonged intubation results in progression of these changes. If the tube is removed early when the ulceration is superficial, healing and re-mucosalization are rapid. Deep ulceration will frequently be appreciated as "ulcerated troughs". These can be seen only after removal of the endotracheal tube and appear as wide, deep erosions through the perichondrium and into the cartilage on the medial aspect of the arytenoid and cricoid cartilages. The cricoarytenoid joint is often exposed and may become inflamed leading to chronic fibrosis and ankylosis with accompanying dysphonia. Weeks to months after extubation, these ulcerated troughs may heal and be noticed as "healed furrows". (Figure: 13, 14) [1]

Figure 13 [1] : **Figure 14[1]:**

Figure 13- Vocal fold Ulceration.
From: Benjamin and Hollinger.
Ann otorhinolaryngol 2008

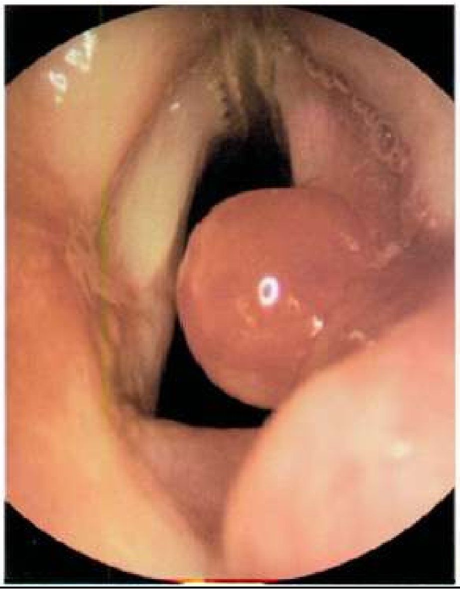


Figure 14- Vocal fold Granulation.
From: Benjamin and Hollinger.
Ann otorhinolaryngol 2008

Ulceration crossing the midline of the posterior glottis with no strip of intact mucosa in the midline signifies a high risk for the formation of posterior glottic stenosis, also known as laryngeal stenosis. The provisional diagnosis of posterior glottic stenosis may be made in patients with a likely history and physical examination that reveals limited abduction of the vocal folds on inspiration with incomplete glottic closure on phonation. Direct laryngoscopy with microscopic examination of the posterior glottis using 0° and 30° telescopes is required for confirmation of this provisional diagnosis. The transverse fibrotic scar appears as a firm, thick web in the posterior glottis between the arytenoid cartilages. The anterior margin may be sharp, localized or blunt. The web may extend from above the interarytenoid area through the level of the glottis and into the subglottic region. Posterior glottic stenosis is unlikely to occur in presence of intact strip of mucosa in the midline. Posterior cricoid split with costal cartilage grafting which can be done endoscopically or via open approach is the treatment of choice for posterior glottis stenosis. [30, 31]

Subglottic stenosis, which is defined as narrowing of the subglottic space above the inferior margin of the cricoid cartilage and below the level of the glottis, is more easily recognized, and may be coexistent with posterior glottic stenosis. Prolonged intubation is the most common cause of subglottic stenosis in both adults and children. The tissue covering the cricoid cartilage area is loose, which makes it more prone to mechanical trauma during intubation and hence inflammatory oedema may cause critical airway compromise. Patients with abnormal cricoid cartilages and congenital subglottic stenosis are more likely to have subglottic complications from intubation. [14]

True vocal cord paralysis may occur as a result of endotracheal intubation. The paralysis is most commonly unilateral, but bilateral paralysis with airway obstruction has been reported. Brandwein et al. examined the course of the anterior branch of the recurrent laryngeal nerve and discovered it to be vulnerable to compression between the inflated cuff of the endotracheal tube, the lateral projection of the abducted arytenoid, and the thyroid cartilage. [18, 32]

EVALUATION OF LARYNX

Visualisation of larynx and pharynx forms an essential part of upper airway examination. It can be done by various methods, simplest being the mirror- indirect laryngoscopy. Prior to 1800, examination of larynx was limited to examination of autopsy specimens. The study about functions of larynx and airway surgery was limited to incising the ‘arteriaaspera’ or ‘rough artery’ as trachea was called by ancient physicians. Guy Babington is cited as the first to have viewed the upper larynx using endoscopic principles. Babington’s “glottoscope,” presented in 1829, was unique in that his was the first instrument to combine the previously separate devices of a reflecting mirror (a common dentist’s mirror) and a tongue depressor into one clinically practical unit. But it was a Spanish teacher Manuel Garcia who first performed indirect laryngoscopy of his own larynx using a dental and a hand mirror using natural sunlight (Figure 15). Since then indirect laryngoscopy mirrors have become an important tool in an otolaryngologist’s armamentarium. Ludwig Turck and Johann Nepomuckczermak in 1858 were the first to perform laryngoscopies on patients. Ludwig also invented the use of artificial light and concave mirror for performing laryngoscopies. Later in 1864-68 efforts of Berlin laryngologists Tobold and Voltolini gave rise to direct laryngoscopy. However, credit for developing and popularising direct laryngoscopy goes to Alfred Kirste, who in 1890s while working with a tubed oesophagoscope (which was a modified urethroscope) accidentally slipped into trachea and realised it an excellent view!! Gustav Killian invented the suspension laryngoscopy while assisting his artist assistant to make pictures of larynx. [17, 33]

Figure : 15

Figure 15 – Manuel Garcia self visualizing the larynx. From: History of Surgery, Knut Haeger. Harold Starke, London 1988.

EVALUATION

The evaluation of a patient for intubation injuries includes a thorough history including indication for intubation, presence of co-morbidities or illnesses, intubation characteristics like date of initial intubation, number of days intubated, failed attempts at extubation re-intubation etc. The mode of intubation (i.e. fiberoptic, blind or with direct laryngoscopy), route of intubation (oral/nasal), use of sedation while intubating and on ventilator in addition to size of tube and presence of naso-gastric tube also to be noted.

Direct laryngoscopy with telescope is considered the ideal method of assessing intubation injuries in the larynx. It provides an excellent magnified image of all areas of larynx and trachea. However, it can be done under general anaesthesia only. Advanced anaesthesia techniques like spontaneous ventilation, assisted ventilation, jet ventilation and apnoea with bag and mask ventilation may be used to evaluate the larynx. Spontaneous ventilation gives the best information and hence is preferred. Child is ventilated with the mixture of Sevoflurane and oxygen via tube kept in oropharynx and additional intravenous anaesthesia is provided by Propofol. Hopkin's rod telescope is passed through a suspended laryngoscope for a clear and magnified image of the airway. [34]

In selected children, flexible laryngoscopy may complement rigid laryngoscopy and both may occasionally be required to evaluate a child's airway adequately. Also, in many instances, these techniques can be used interchangeably. Each technique has its advantages and the method of examination depends on the case. Rigid laryngoscopy provides a superior assessment of the larynx, especially the posterior glottis area. It also allows palpation of arytenoids hence to diagnose the crico-arytenoid joint dislocation or any other cause for vocal cord immobility. Flexible laryngoscopy is often extremely valuable in assessing larynx that is difficult to access with rigid instrumentation and may provide valuable information about airway dynamics, such as vocal cord mobility, the degree of pharyngeal collapse, glossoptosis and the presence of laryngomalacia and tracheomalacia. [34] However, Flexible laryngoscopy has its limitations. The image is not clear as that obtained by a rigid telescope. Hence, small lesion or early changes may be missed. Sometimes a thorough assessment of the posterior larynx may not be possible. Most of the intubation trauma occurs at this region. Also, a complete assessment of inter-arytenoid and subglottic region is seldom possible. [23, 24]

Imaging also plays important role in paediatric airway assessment. It can be done before or after the endoscopic evaluation. A chest and neck radiographs both lateral and anterior/posterior views assesses concomitant respiratory injuries or secondary effects of upper respiratory tract obstruction on the lower airway. [35]

Videostrobolaryngoscopy (VSL) is also useful in this regard if the patient is able to tolerate the procedure. Alessi et al. found VSL to be quite valuable in the documentation of intubation trauma and were successful in performing the examination at the bedside in critically ill patients. [36]

Barium swallow is helpful in evaluating reflux and risk of aspiration. It is mainly indicated in evaluation for posterior laryngeal cleft or trachea-oesophageal fistula. [37]

CT scan and MRI for airway assessment offer a complimentary tool to endoscopic evaluation of the larynx and trachea. CT scans can provide anatomic information, such as the length of a stenosis; however, they cannot differentiate between the true lumen and overlying secretions, which introduce inaccuracies in the presence of blood, mucus and crusting. CT scan using helical or electron beam scanners can be used to generate ‘virtual’ bronchoscopic images, keeping it just one step short of direct visual examination. High definition scans are expensive and introduce a high dose of radiation, making them unsuitable for long term monitoring of patients, and often requires sedation in children.MRI scans have a slight edge over CT scans in showing the soft tissue details of the stenosis. [6, 38] However, they are not usually done as a primary modality in evaluating the larynx.

ASSOCIATED RISK FACTORS

Multiple risk factors are found to contribute in developing complications after intubation. Absolute correlations between coexistent illnesses and particular types of injury have not been proved. Abnormal anatomy, multiple intubations, lack of skill of the intubator and difficult laryngoscopy may predispose to physical trauma during the act of intubation. Inflamed larynges are more prone to injury, as in acute laryngotracheobronchitis or in cases of burns where the inflammatory response already present within the larynx makes the mucosa more susceptible to pressure necrosis. [39]

Several characteristics of the tube itself may predispose to greater injury. Size of the tube is important in determining the extent of injury. Some authors suggest that the upper limit of inside diameter of the endotracheal tube (ETT) be 8.0 mm in males and 7.0 mm in females. Santos et al. recommends that prolonged intubation with a tube larger size tube should be avoided. They demonstrated that there was an increased incidence of vocal fold immobility after extubation in patients who had prolonged intubation with a tube greater than 7.5 mm. Infants and children less than 8 years old should have an uncuffed tube that allows for an air leak with 20 cm of water positive pressure. [40] Even with an appropriately sized endotracheal tube, excessive motion which may occur as a result of patient movement, motion transmitted from the ventilator or manipulation during suctioning of the tube may induce repeated trauma. Even though, high-volume, low-pressure cuffs have replaced the high-pressure cuffs used in the past, a highly inflated cuff may still induce excessive trauma within the larynx.

Gastroesophageal reflux and aspiration are common in critically ill patients. This repetitive bathing of the laryngeal structures with gastric acid causes a chemical irritation that adds to the local injury from the endotracheal tube. [41] It may be beneficial to use H_2-blockers to minimize reflux in critically ill and intubated patients.

The presence of a nasogastric (NG) tube increases the likelihood of reflux. Nasogastric tubes may also cause irritation and ulceration in the post-cricoid region and have been reported to cause cricoid chondritis. Friedman et al. concluded after examining many patients that presence of nasogastric tube can cause chondritis of cricoid cartilage. [41] They found localized odynophagia and pain radiating to the ear to be attributable to mucosal ulceration. These patients had nasogastric tube for longer than three days, often positioned in the midline. They thus recommend that patients with nasogastric tubes, who experience pain, have the tube for longer than three days or who are unconscious receive anteroposterior neck radiographs. If the nasogastric tube is positioned in the midline, it should be re-positioned laterally. If symptoms persist, laryngoscopy should be performed to rule out cricoid chondritis. If any sign of inflammatory reaction is seen in postcricoid region, it should be addressed aggressively by starting intravenous broad spectrum antibiotics.

Injury to the cricoid cartilage can occur due to presence of endotracheal tube alone or in conjunction with a nasogastric tube. Simultaneous presence of both may accentuate the insult and result in the formation of fistula, which can be difficult to treat. [41, 42]

Chronic diseases may also predispose the patient to intubation trauma. Medical conditions associated with decreased tissue perfusion increase the likelihood of tissue necrosis and ulceration. These conditions include congestive heart failure, liver failure, hypoxemia and anaemia. Gaynor and Greenberg noted a very high incidence of severe complications in patients with insulin dependent diabetes mellitus and they recommend early tracheotomy in these patients if the length of intubation is expected to exceed four days because by this time there may occur bacterial colonization and biofilm formation. [43, 44] Immunocompromised patients are more prone to bacterial infection of mucosal ulcerations and should be monitored closely for the development of chronic chondritis and its sequelae. In patients with any of these co-existing illnesses, early tracheotomy should be considered. [44]

Laryngeal intubation can cause minor or major injuries. Overall outcome depends upon various factors like type and size of tube, characteristics of intubation, presence of GERD, nasogastric tube or any other co-morbidity including quality of nursing care given to the patient. [45]

Lindholm in 1969 proposed a classification system based upon the findings of direct laryngoscopy. [6]

Grade I: Oedema and hyperaemia without ulceration.

Grade II: Superficial ulcer involving less than one third of the circumference of the airway Grade III: Superficial ulcer involving more than one third of the airway / deep ulcer less than one third.

Grade IV: Continuous deep ulceration of more than one third of the circumference of the airway / deep ulcers in the mucosa with exposure of cartilage. [6]

Ratna Thomas et al in 1985 [46] suggested another simplified and easy to apply classification which was based on endoscopic findings in larynx and trachea immediately after extubation in adults.

Grade 0: Normal mucosa

Grade 1: Erythema and/or oedema but no ulceration

Grade 2: Ulceration and/or slough but no narrowing of airway

Grade 3: Glottic or subglottic narrowing due to oedema and/or slough

Grade 4 : Vocal fold paralysis. [46]

MATERIALS AND METHODS

Children who underwent endotracheal intubation from 1st September 2011 to 30th November 2012 were included in the study. Parents or caregivers of children who underwent intubation as an emergency, semi-elective or elective procedure, and were admitted in the Paediatric Intensive Care Unit for 48 hours or more, were invited to participate in the study. Informed consent was obtained from the parent or guardian when extubation was planned.

Patient selection criteria-

Inclusion Criteria:

Children who were admitted to the Paediatric ICU with

- endotracheal tube in situ for more than 48 hours
- Age 1-15 years
- Consent from the parent or guardian to participate in the study

Exclusion criteria - presence of any of the following conditions:

- Congenital abnormality of the respiratory tract
- Thyroid surgery, cardiothoracic surgery, and/or neck trauma
- Needing oxygen therapy of fio2 >60%

- Extubation to NPCPAP/high flow oxygen therapy
- Requiring more than one ionotrope
- Respiratory Rate > 2 SD above normal for age
- HR> 2 SD above normal for age
- Platelet count < 50,000/cu.mm
- Evidence for coagulopathy (INR> 1.5)
- Head injury (possibility of ICP still being high)
- Acute neuroinfections/ status seizures if GCS < 10
- Any other in the opinion of the ICU senior consultant felt to be unfit for procedure.

After obtaining consent, the details of the medical condition, course during ICU stay and characteristics of intubation, like indication for intubation, type and size of the endotracheal tube, intubator, number of attempts, difficult or traumatic intubation etc. were collected from the IP chart, in-charge nursing staff and ICU personnel. Information about presence of any co-morbidities like abnormal shape of larynx, anaemia, hypotension, presence of any respiratory disease etc. which might affect the outcome of the laryngeal injuries were recorded from the medical records. Details of parameters like duration of intubation and ventilation, presence of naso-gastric tube, use of sedation, trauma due to suction cleaning were documented.

Flexible laryngosopy:

A flexible nasolaryngoscopy was performed in the ICU setting within 24 hours of extubation. Examination was performed at the bedside with the child in supine position without any hyperextension of the neck. During the procedure, cardiac monitoring and pulse oximetry were maintained. The nose was decongested with 0.05% xylometazoline paediatric nasal drops prior to the procedure. (Figure: 16) A flexible laryngoscope of 3.7mm x 34cm size (Karl Storz) was used to perform the procedure. (Figure: 18 & 19) The fibre-optic scope was connected to the camera, monitor and a recording system to record the images. (Figure: 20) 2% lignocaine jelly was applied over the anterior nare and also around the terminal end of the scope for smooth and atraumatic passage of the scope through the nose. If a nasogastric tube was in place, the scope was introduced though the other nostril. Flexible scope was passed along the floor of the nasal cavity to reach the laryngopharynx through the nasopharynx. The tip of the scope was rested at the level of the epiglottis to visualize/ examine the glottis and the immediate subglottis. Contact of the instrument with any of the laryngeal structures was avoided due to the risk of developing spasm. The procedure was conducted in presence of intensive care doctors who were capable of handling any untoward complication like spasm. The whole procedure was recorded, and reviewed independently by 2 observers. The findings were noted in a proforma designed for the study.

A repeat laryngoscopy was performed under local anaesthesia after 3-4 weeks in the ENT OPD and findings documented. (Figure: 17)

The presence and degree of laryngeal pathologies were documented and graded as 0,1,2 or 3, indicating none, mild, moderate, and severe injuries, after reviewing the recorded images(see in proforma).

-Erythema was defined as excessive redness and congestion of the larynx.

-Oedema is an excessive accumulation of serous fluid in the intercellular spaces of tissue. It was graded de[ending on the swelling of the laryngeal structures.

- Granulation tissue was defined as protruding, inflamed, fibrovascular tissue in the region the vocal process.

- Ulceration was defined as a loss of tissue in this same region.

- Vocal fold immobility was rated as not present (i.e., normal mobility), mild (barely perceptible decreased motion), moderate (obvious decreased movement but not immobile), or severe (no vocal fold movement seen).

The child was monitored during, and twenty minutes after the procedure to identify any complications. The complications were categorized as minor and major. Minor complications included laryngospasm not requiring ventilation, drop in oxygen saturation, but not below 85%, with rapid recovery, and minor nasal bleeding. Major complications included desaturation below 85%, bradycardia and laryngospasm requiring ventilation.

Statistical method:

Analysis was done using SSPS statistics – version 21. Individual types of laryngeal injury like oedema, erythema, ulceration, granulation tissue, vocal fold immobility and subglottic stenosis were correlated to age, size and type of tube, duration of intubation and skill level of the intubator.

For the test between the continuous (duration) predictors and outcomes (injury), Mann-Whitney Test was used because the duration is not normally distributed.

For the test between the continuous (size of the tube) predictor and outcomes (injury), independent sample t- Test was used because the size of the tube is normally distributed.

For the test between the continuous (intubator) predictor and outcomes (injury), independent sample t- Test was used because the intubator is normally distributed.

For the tests between categorical predictors and outcomes, simple $\chi 2$ (chi-square) test was used.

Figure: 16

Figure: 17

Figure: 18

Figure: 19

Figure: 20

RESULTS AND ANALYSIS

A total of thirty-four (n=34) patients who were admitted in paediatric ICU, met the inclusion and exclusion criteria and were included in the study after taking informed consent from the parents/caretakers.

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I. AGE AND SEX DISTRIBUTION

Table 2: Age distribution of study patients (n=34)

Age	Frequency	%
1-5yrs	19	56%
6& above	15	44%

Table 3: Sex distribution (n=34)

Sex	Number	%
Male	18	53%
Female	16	47%

The age ranged from one year to fifteen years with a median age of 4 years. Nineteen patients (53%) were under five years of age, while the remaining fifteen were six years and above (44%).

There were eighteen (53%) male patients and sixteen (47%) female patients.

II. INDICATION FOR INTUBATION

Table 4: Indication for intubation

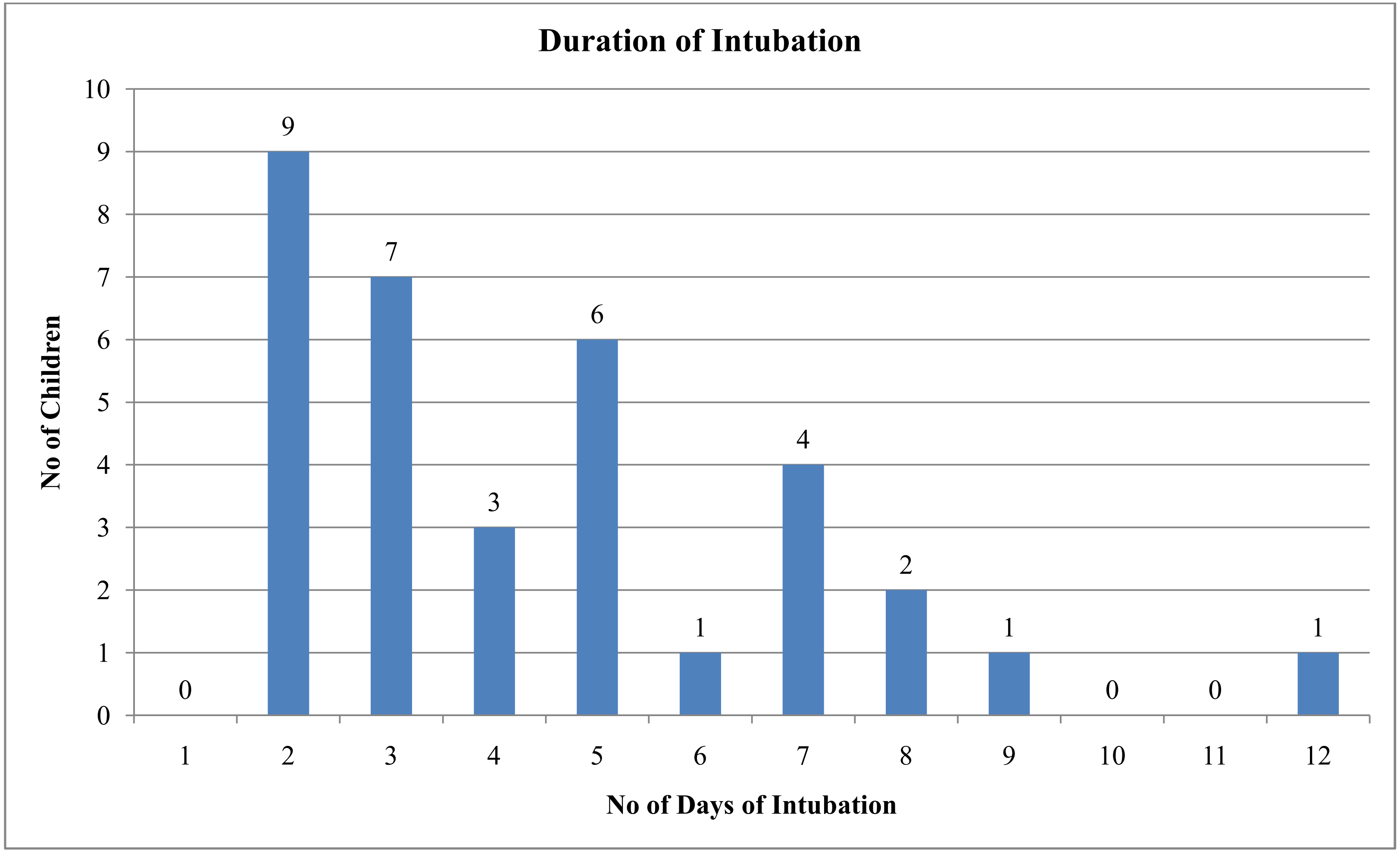
Primary Pathology	**No.**
Infective	12
Primary Neurogenic	6
Poisoning	6
Gastrointestinal	5
Renal	2
Neuromuscular	1
Storage Disorder	1
Orthopedic Trauma	1
Total	34

Infection was the commonest indication for intubation. Twelve children were intubated due to infection. Of these seven children were diagnosed with Dengue fever, three with viral meningoencephalitis, one with meningitis and one with pneumonia. Neurogenic causes and poisonings were also common indication for intubation with six children in each group. Status epilepticus was the commonest neurogenic indication, seen in three children. Of the two children intubated following consumption of organophosphate poisoning, one was tracheostomized. Five children were intubated due to a gastro-intestinal pathology and two due to a renal pathology**.**

III. DURATION OF INTUBATION

Children intubated for at least 2 days were included in the study. Duration of intubation varied ranging from minimum of 2 days to maximum of 12 days with median of 4 days. Majority of children i.e., twenty five were intubated for a period of five days or less. While eight children were intubated for six to ten days and only one child was intubated for a period of more than ten days. A 1 year old child with meningoencephaitis was intubated for 12 days.

Figure 21: Duration of intubation



IV. SIZE OF ENDOTRACHEAL TUBE

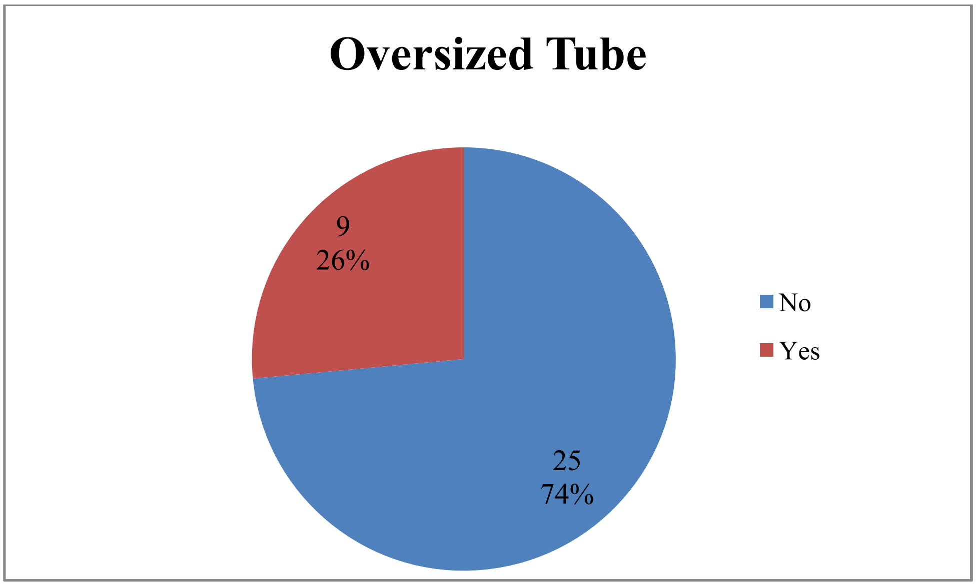
Table 5: Size of the Endotracheal Tube

Size of tube(mm)	Frequency	Percent(%)
≤ 4mm	7	20.6
4.5mm - 6mm	20	58.8
>6mm	7	20.6

A wide range of tube sizes were used in the study group, varying from 3.5 to 7 mm. Twenty children were intubated with a endotracheal tube sized between 4-6mm (59%). Seven children (20.6%) were intubated with an endotracheal tube of size 4.0 mm and below and seven children (20.6%) with an endotracheal tube size above 6.0 mm.

V. USE OF OVERSIZEDENDOTRACHEAL TUBE

Figure 22: Use of oversized endotracheal tube



No standardized recommendations for tube size are available for the Indian population, though the generally accepted principle is that the endotracheal tube should not be larger than two thirds of the tracheal diameter. We used the Pennlington's formula (age/4 + 4 for uncuffed and age/4 + 3.5 for cuffed endotracheal tube) to calculate the ideal size of the endotracheal tube. The endotracheal tube used was compared to the ideal to decide if the tube used was of appropriate size or was oversized. In more than a quarter of the children (26%) and apparently oversized tube was used. These children with apparently oversized tubes were on a larger tube due to high pressures required for ventilation.

VI. TYPE OF ENDOTRACHEAL TUBE

Figure 23: Type of endotracheal tube

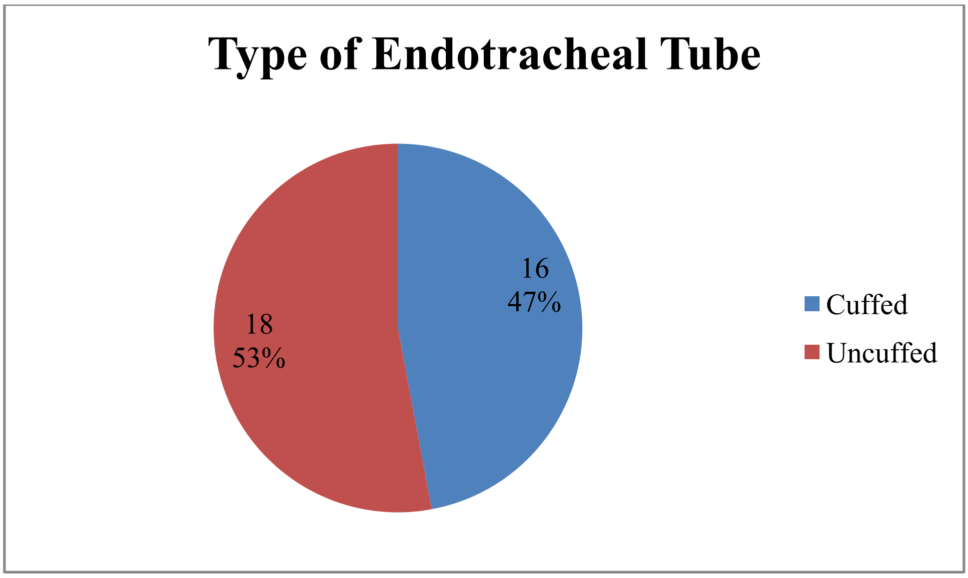
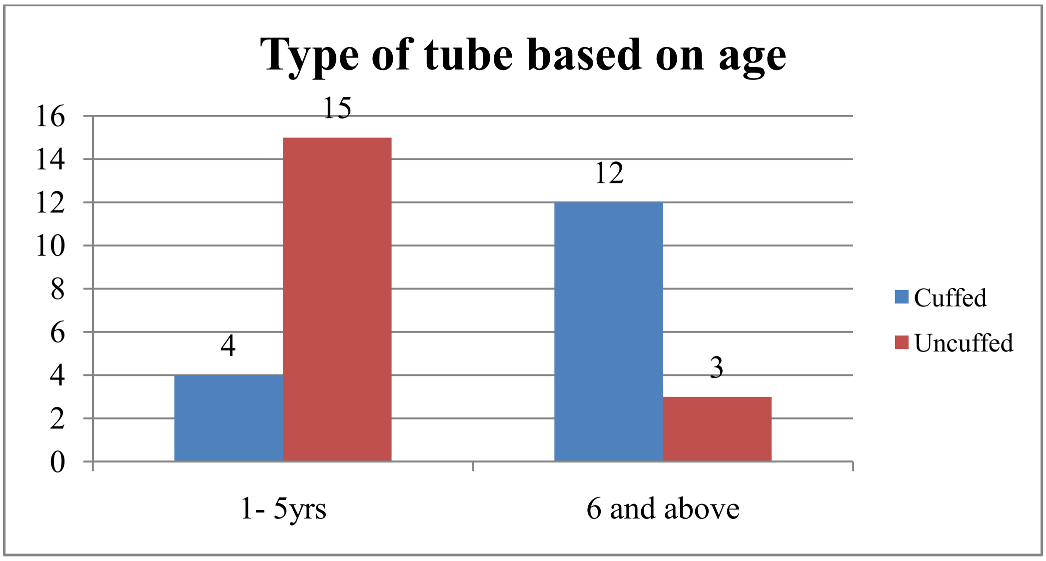


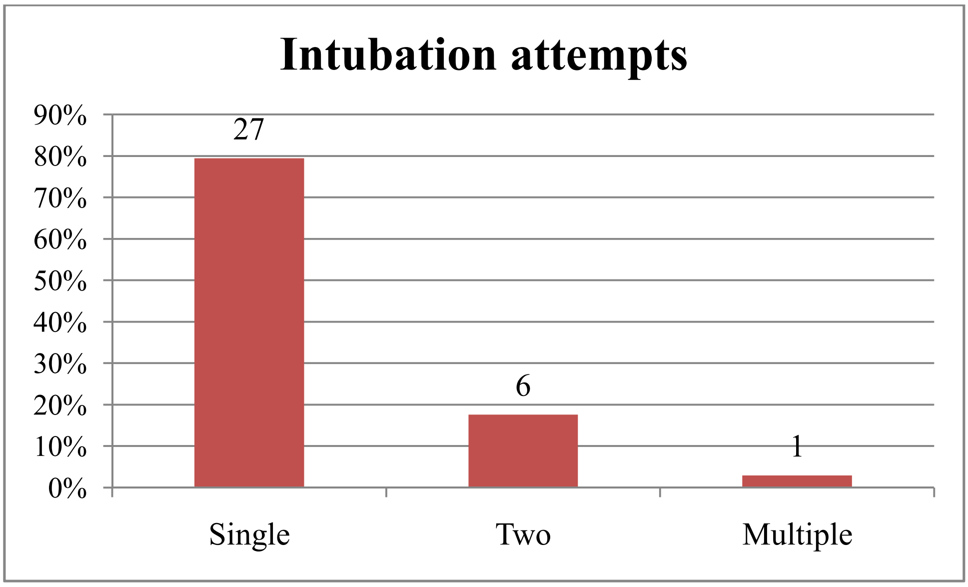
Figure 24: Type of tube based on age of the child



There was almost equal distribution in use of cuffed (53%) and uncuffed (47%) endotracheal tubes in the children included in the study. Older children tended to have cuffed tubes with all but three children over five years having a cuffed tube. However in the under five age group, only four out of nine children had cuffed tubes.

VII. INTUBATION ATTEMPTS

Figure 25: Intubation attempts



Majority of intubations were successful in a single attempt. Twenty seven children (79.4%) were intubated in a single attempt. Six children (17.6%) were intubated in two attempts and one child required multiple attempts of intubation (3%). The child with multiple attempts of intubation was a difficult emergency intubation in casualty.

VIII. TIME TAKEN TO INTUBATE

Table 6: Time taken to intubate

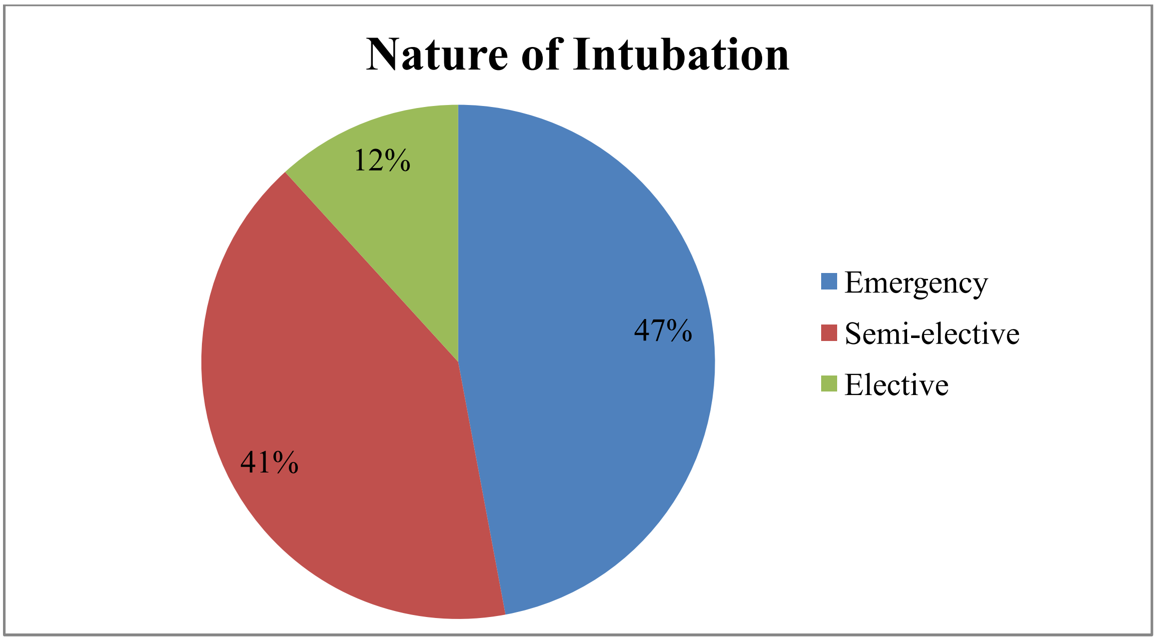
Time Taken	No	%
< 30 sec	20	58.8
30 sec to 60 sec	14	41.2
> 1min	0	0

In twenty children (58.8%), it took less than 30 seconds to intubate, while in fourteen patients (41.2%), it took 30-60 seconds to intubate the child. None of the intubations exceeded more than a minute.

IX. NATURE OF INTUBATION

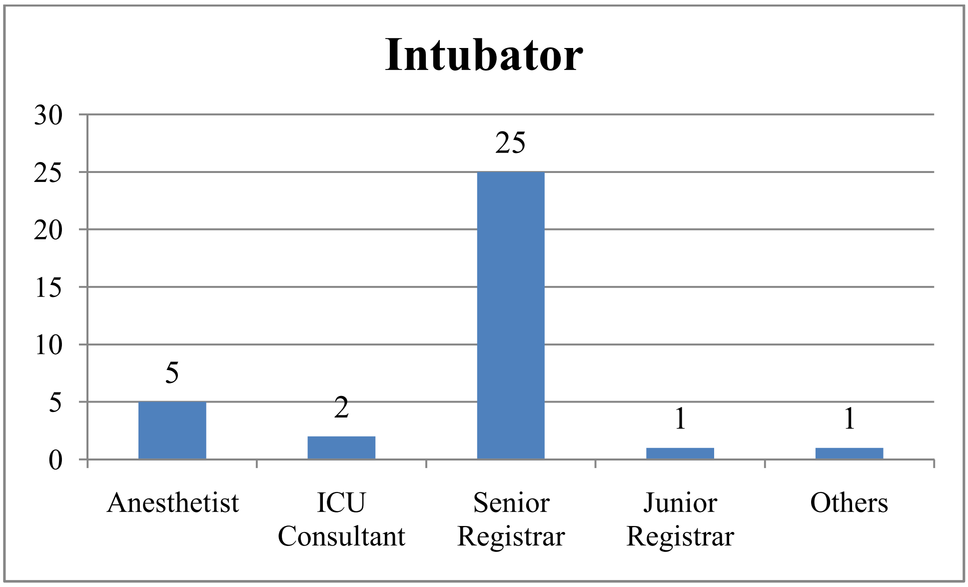
Sixteen intubations (47.1%) were emergency intubations, while fourteen intubations were done as semi-elective procedure (41.2%). The only four intubations were elective (12%). Majority of the emergency intubations were in paediatric casualty and by the casualty registrar.

Figure 26: Nature of intubation



X. SKILL LEVEL OF INTUBATOR

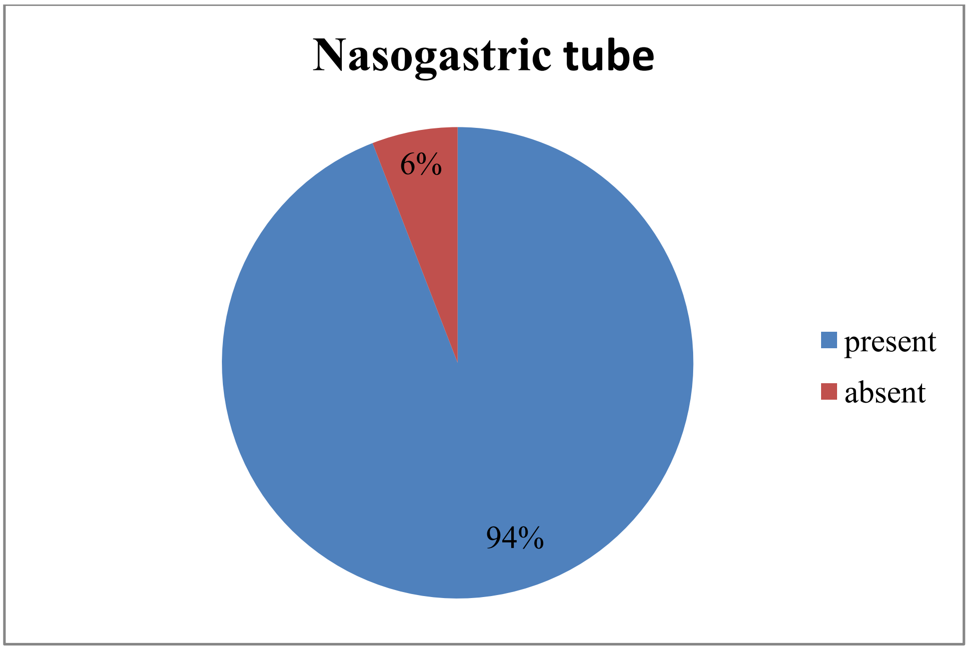
Figure 27: Skill level of intubator



Majority of the intubations (73%) were done by a senior registrar. Five (15%) intubations were done by anaesthetist, two (6%) by paediatric intensive care consultant and one child (3%) by a junior registrar. One child (3%) was intubated outside the hospital and brought to the hospital as a tertiary referral. The intubators were re-grouped as expert and novice intubators for better statistical comparison. Anaesthetists and paediatric ICU consultants were considered as 'Expert Intubators' whereas registrars (senior and junior) and outside intubations were considered as 'Novice Intubators'.

XI. NASOGASTRIC TUBE

Figure 28: Nasogastric tube



Nasogastric tube was present in almost all the children (94%).

XII. TRACHEOSTOMY

Only one child in the study group of thirty-four children under went tracheostomy. This was a child who had organophosphorous poisoning and was ventilated for seven days. The child had post extubation stridor and endoscopic assessment showed significant subglottic granulation. Endoscopic debridement of subglottic granulations was done after a prophylactic tracheostomy. The child was followed up and successful decannulation was done after two weeks.

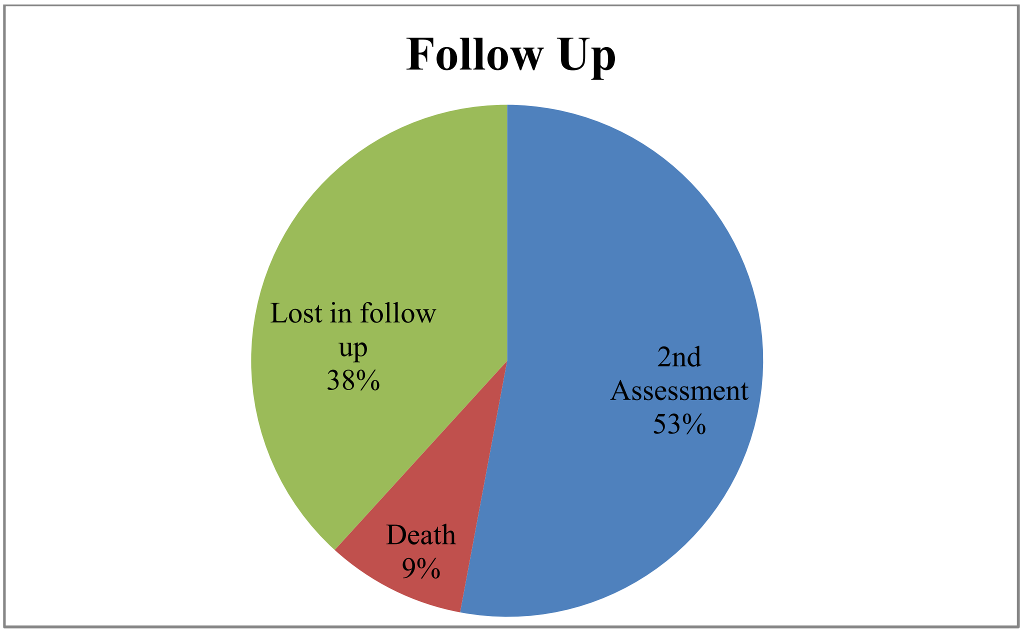
XIII. COMPLICATIONS

Two patients had minor nasal bleed which subsided with pressure and oxymetazoline 0.025% nasal drops. There were no desaturations recorded with oxygen saturation being maintained above 92% in all patients. Two patients needed reintubation, one of whom needed a tracheostomy.

XIV. FOLLOW UP

Initial assessment was done on all the thirty-four patients. Follow up endoscopy after 3-4 weeks was done on eighteen patients. Three children died due to complications of their primary problem while four children, from other parts of country couldn’t come back for follow up. Six children did not return for follow up as were being treated elsewhere for the primary pathology. Three children were lost on follow up and were untraceable.

Figure 29: Follow up



XV. SPECTRUM OF LARYNGEAL INJURES

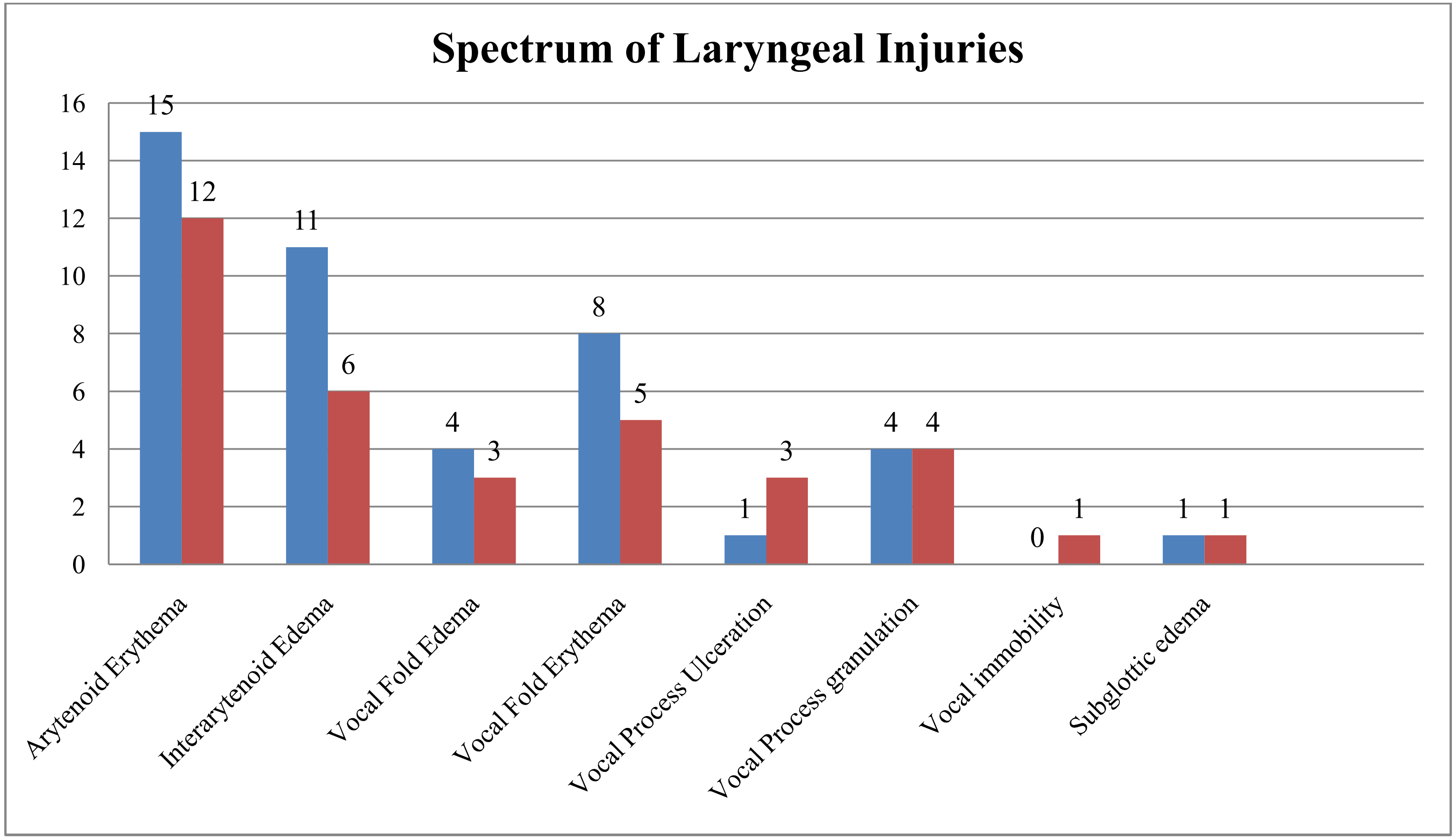
Majority of the injuries had resolved on follow up endoscopy. Arytenoid oedema had fully resolved from initial of twenty-six (77%), arytenoid erythema from twenty eight (82%) to one (3%). Complete resolution was seen in inter-arytenoid oedema from initial seventeen (50%). Similarly vocal fold oedema , vocal fold erythema, vocal Process ulceration and vocal fold immobility resolved completely from initial of eight(24%), twelve(35%) seven(20%) and one (3%) respectively. Vocal process granulation resolved from ten (29%) to one (3%). Subglottic narrowing was seen in two patients which remained the same on follow up. On reviewing the data on subglottic narrowing, one of the two children with subglottic narrowing resolved completely after four weeks while the other progressed into subglottic stenosis. One child who had apparently normal subglottis on initial assessment during immediate post-extubation subsequently developed subglottic narrowing after 3- weeks.

For more comprehensive understanding of the pathogenesis of laryngeal injuries, the above findings were re-grouped based on the degree of laryngeal injury. Arytenoid oedema, inter-arytenoid oedema and vocal fold oedema are similar in terms of degree of injury and were clubbed together as 'laryngeal oedema'. Similarly arytenoid erythema and vocal fold erythema were grouped as 'laryngeal erythema'. Right and left vocal process ulcerations were unified as laryngeal 'ulceration' and similarly right and left vocal process granulations were combined as 'granulation'. Vocal fold immobility and subglottic oedema/narrowing were retained.

Table 7: Spectrum of Laryngeal Injuries

	1st Scopy	Follow Up scopy
Arytenoid Oedema	26	0
Arytenoid Erythema	28	1
Interarytenoid Oedema	17	0
Vocal Fold Oedema	8	0
Vocal Fold Erythema	12	0
Vocal Process ulceration	7	0
Vocal Process granulation	10	1
Vocal immobility	1	0
Subglottic Oedema	2	2

Figure 30: Spectrum of Laryngeal Injuries



XVI. LARYNGEAL INJURIES - AGE DISTRIBUTION

For statistical comparison, patients were grouped into two groups; ‘Group 1’ - children below or equal to five year and ‘Group 2’children six years and above. There were nineteen patients in group 1 and fifteen patients. Group 2

Laryngeal oedema and laryngeal erythema were the commonest findings in both the groups. Laryngeal oedema consisted of 79% and 87% in group 1 and 2 respectively and laryngeal erythema 74% and 91% respectively.

Table 8: Age distribution of laryngeal injuries

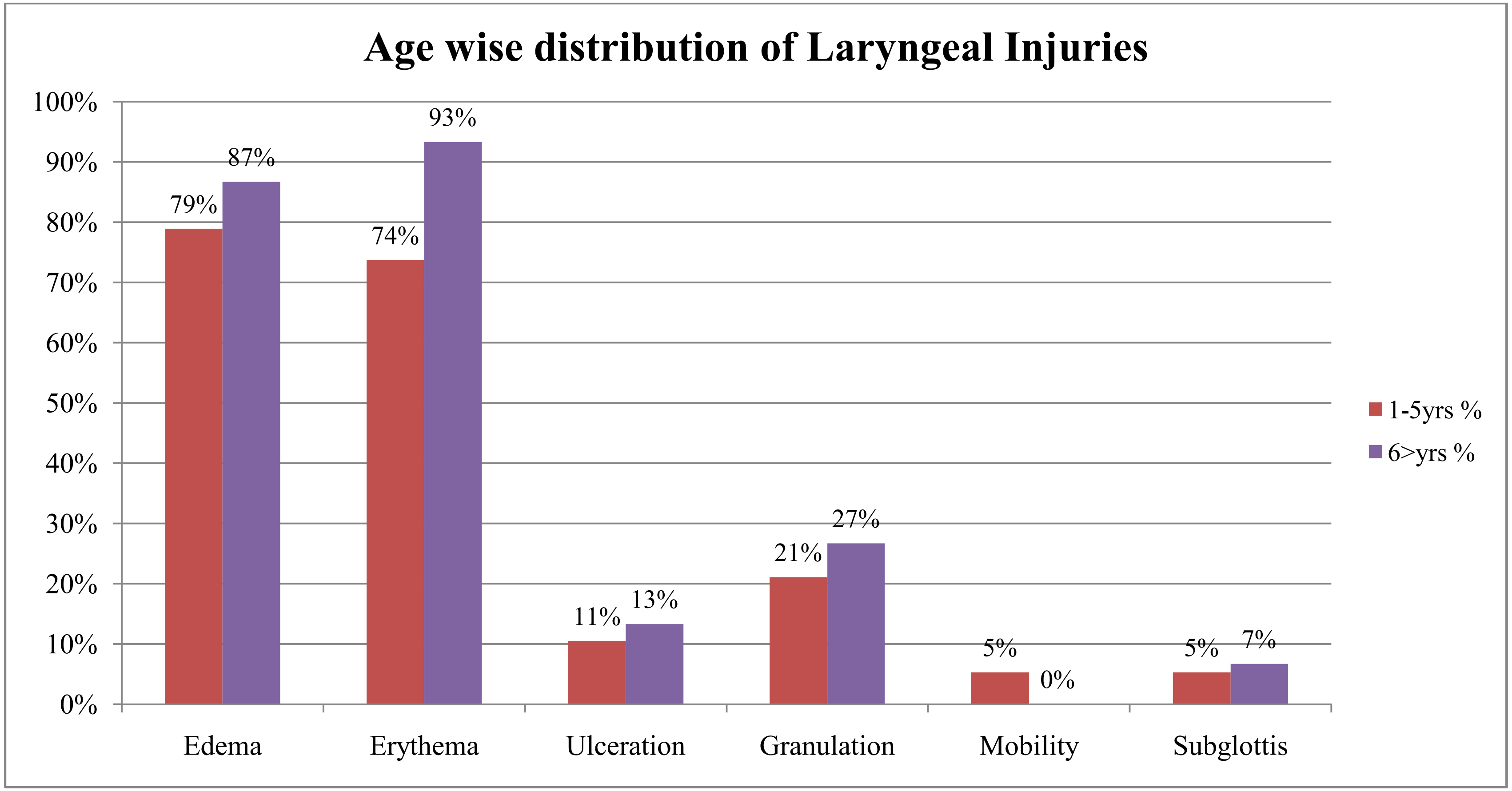
	Oedema	Erythema	Ulceration	Granulation	Mobility	Subglottis
1-5 yrs	15	14	2	4	1	1
1-5yrs %	79%	74%	11%	21%	5%	5%
6>yrs	13	14	2	4	0	1
6>yrs %	87%	93%	13%	27%	0%	7%

Laryngeal ulceration and granulations were proportionately higher in children six years and above. Laryngeal ulceration was 11% in group 1 and 13% in group 2.Laryngeal granulation were 21% and 27% in group 1 & 2 respectively.

These findings show an increased incidence of laryngeal injury across the spectrum i.e., oedema, erythema, ulceration and granulation in children six years and above i.e., group 2. The numbers for vocal fold immobility and subglottic narrowing were too small to be significant.

Chi-square test using Fischer's exact test was used to calculate the 'p-value' to establish the relationship between age and laryngeal injuries. The p values for oedema (0.564), erythema (0.196), ulceration (0.603), granulation (0.506), vocal fold immobility (0.559) and subglottic narrowing (0.695) were not statistically significant.

Figure 31: Age distribution of laryngeal injuries



XVII. LARYNGEAL INJURY BY DURATION OF INTUBATION

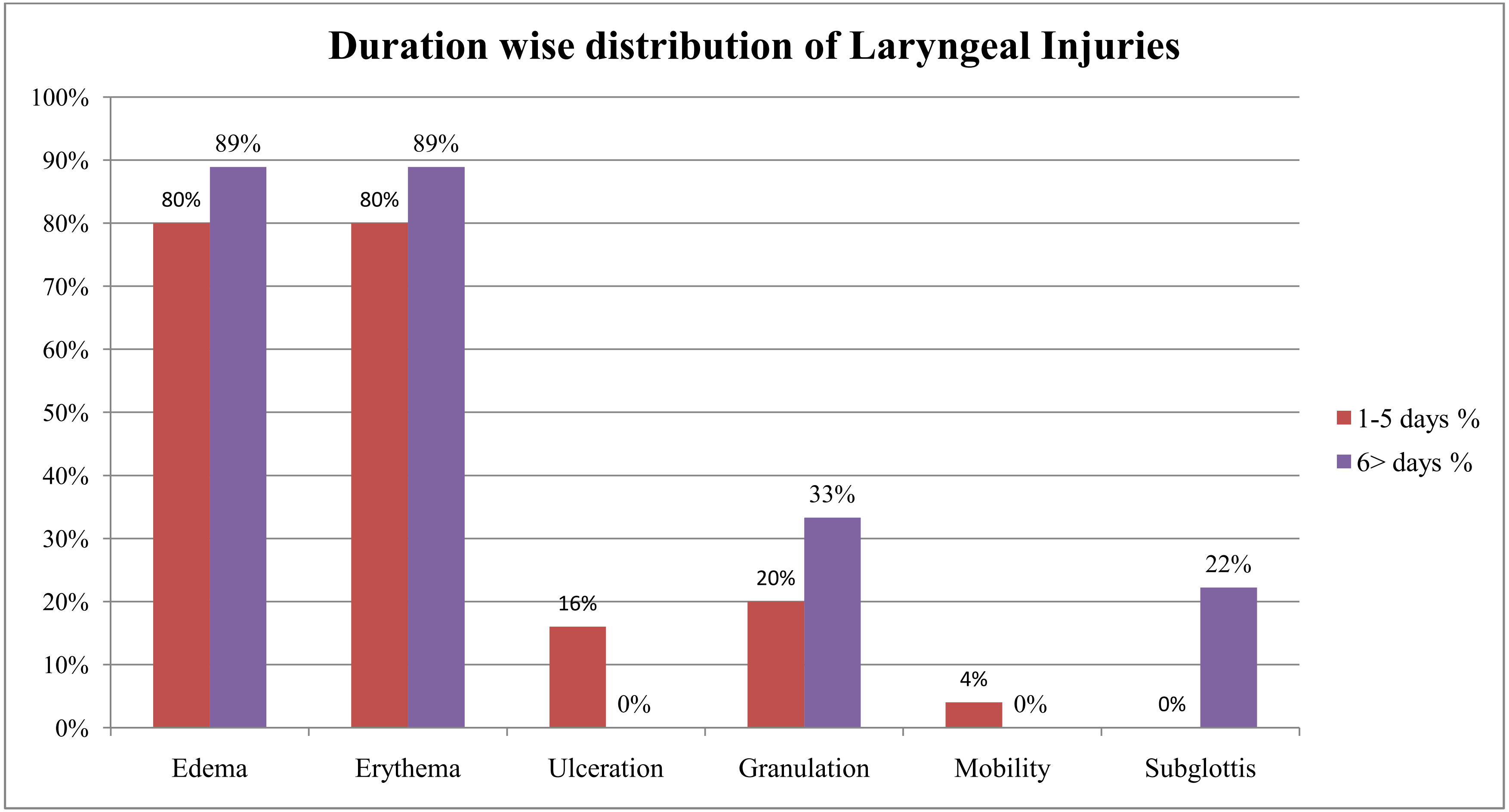
Table 9: Laryngeal Injury by duration of intubation

	Oedema	Erythema	Ulceration	Granulation	Mobility	Subglottis
1-5 days	20	20	4	5	1	0
1-5 days %	80%	80%	16%	20%	4%	0%
6> days	8	8	0	3	0	2
6> days %	89%	89%	0%	33%	0%	22%

Most of the children were intubated for less than five days. For statistical comparison, children were categorized into two groups: children intubated for five days or less as group 1 and children intubated for more than five days as group 2. There were twenty-five children in group 1 and nine children in group 2.

Laryngeal oedema and laryngeal erythema was the commonest finding in both the groups, 80% each in group 1 and 89% each in group 2. Laryngeal ulceration was present in four patients in group 1, but was absent in group 2. Laryngeal granulations were seen in 20% children in group 1 and 33% children in group 2. Vocal fold immobility was seen in one child in group 1. Subglottic narrowing was seen in group 2 only, i.e., children intubated for more than five days.

Figure 32: Laryngeal Injury by duration of intubation



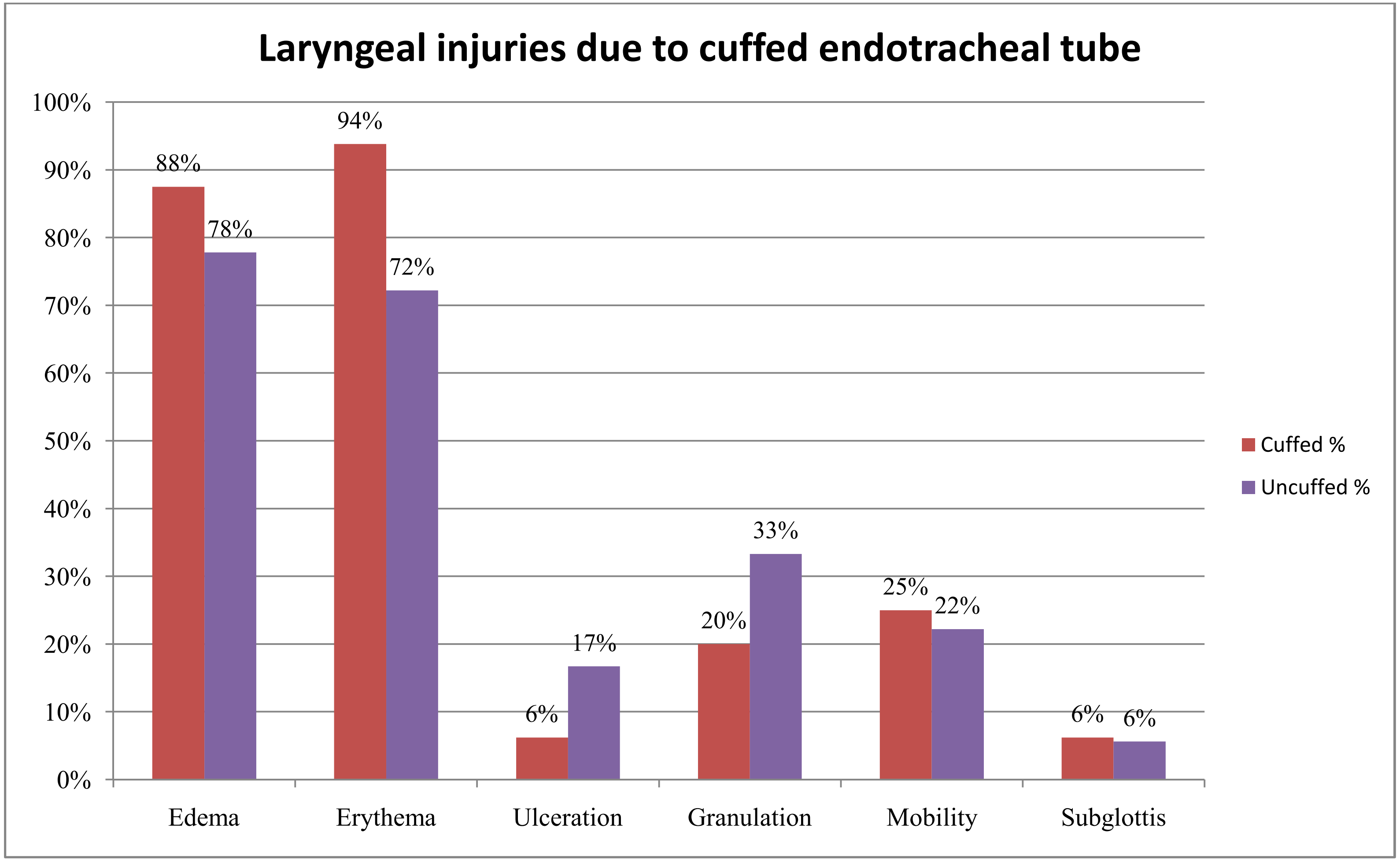
Chi-square test using Fischer method was used to establish relationship between duration of intubation and laryngeal injuries. The p values for oedema (0.487), erythema (0.487), ulceration (0.351), granulation (0.375), and vocal fold immobility (0.735) were not statistically significant. Subglottic narrowing (0.064) although not statistically significant showed an increasing trend with the number of days of intubation.

XVIII. LARYNGEAL INJURIES DUE TO CUFFED ENDOTRACHEAL TUBE

Table 10: Laryngeal injuries due to cuffed endotracheal tube

	Oedema	Erythema	Ulceration	Granulation	Mobility	Subglottis
Cuffed	14	15	1	5	4	1
Cuffed %	88%	94%	6%	20%	25%	6%
Uncuffed	14	13	3	3	4	1
Uncuffed %	78%	72%	17%	33%	22%	6%

Figure 33: Laryngeal injuries due to cuffed endotracheal tube



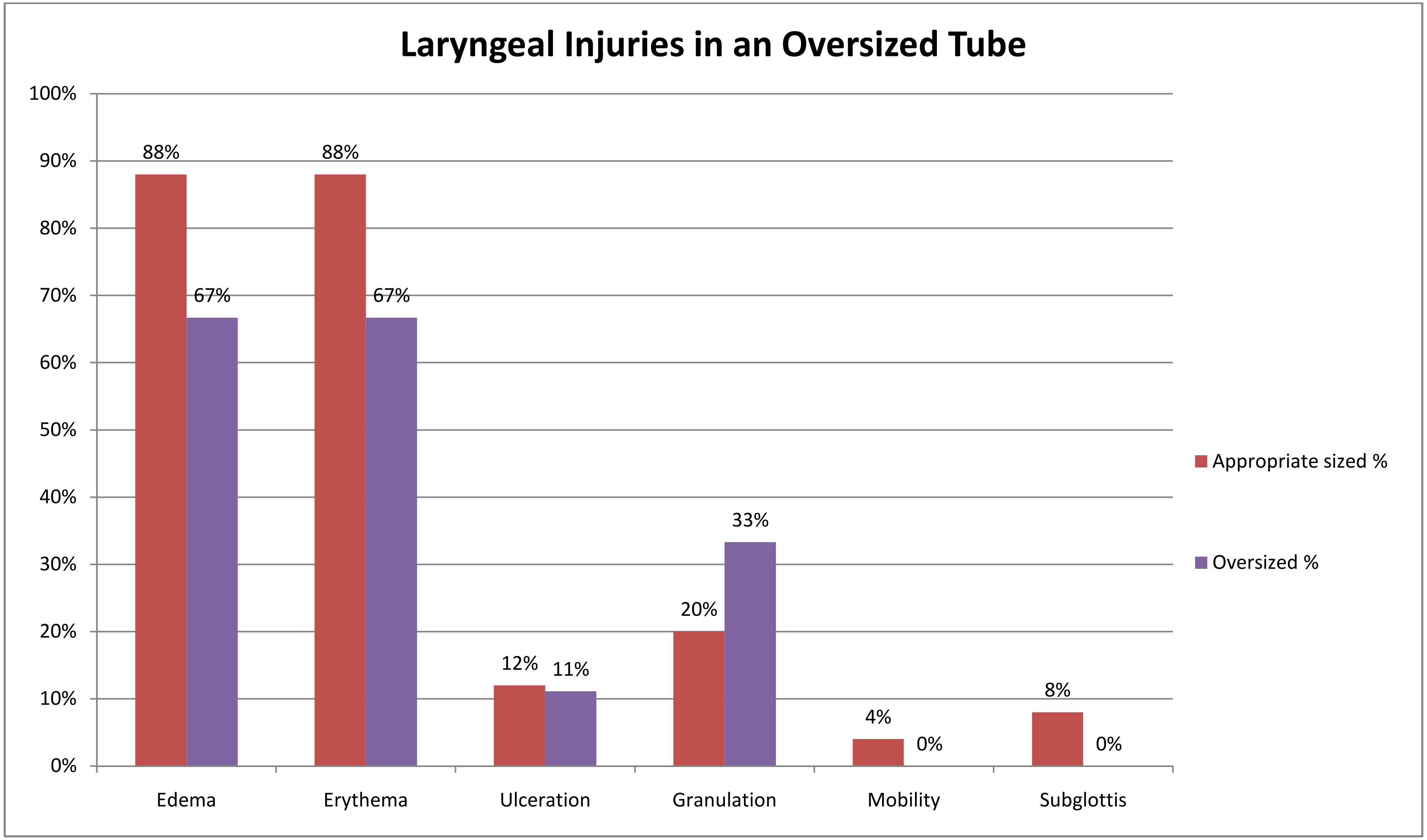
In the study group of thirty-four children, sixteen children were intubated with a cuffed tube and eighteen were on an uncuffed tube. Oedema and erythema were commonly seen in both groups with no statistical difference. In the group of children with cuffed tube oedema was seen in 88% compared to 78% in uncuffed (p=0.389). Erythema was present in 94% in cuffed while 72% in uncuffed (p=0.180). Ulceration was seen in 6% and 17% respectively. (p=0.348) Granulations were also more common with uncuffed tubes although the values were not statistically significant (p=0.583).

XIX. LARYNGEAL INJURIES IN OVERSIZED TUBE

Table 11: Laryngeal injuries in oversized tube

	Odema	Erythema	Ulceration	Granulation	Mobility	Subglottis
Appropriate sized %	22	22	3	5	1	2
Appropriate sized %	88%	88%	12%	20%	4%	8%
Oversized	6	6	1	3	0	0
Oversized %	67%	67%	11%	33%	0%	0%

Figure 34: Laryngeal injuries in oversized tube



Based on the Pennlington's formula, nine patients were intubated with an apparently oversized tube. Laryngeal oedema and erythema was present in 67% of children with apparent oversized tube compared to 88% in children with appropriate sized tube (p=0.174). Laryngeal ulceration were seen in 11% compared to 12% in children with appropriate sized tube (p=0.719). Granulations were seen 33% children with oversized tube compared to 20% children with appropriate sized tube (p=0.351). Vocal fold immobility and subglottic narrowing were not seen in the group with an oversized tube. There was no statistically significant lesion in the oversized tube group. This may be because of the relatively short duration of intubation or the small number of patients in this group

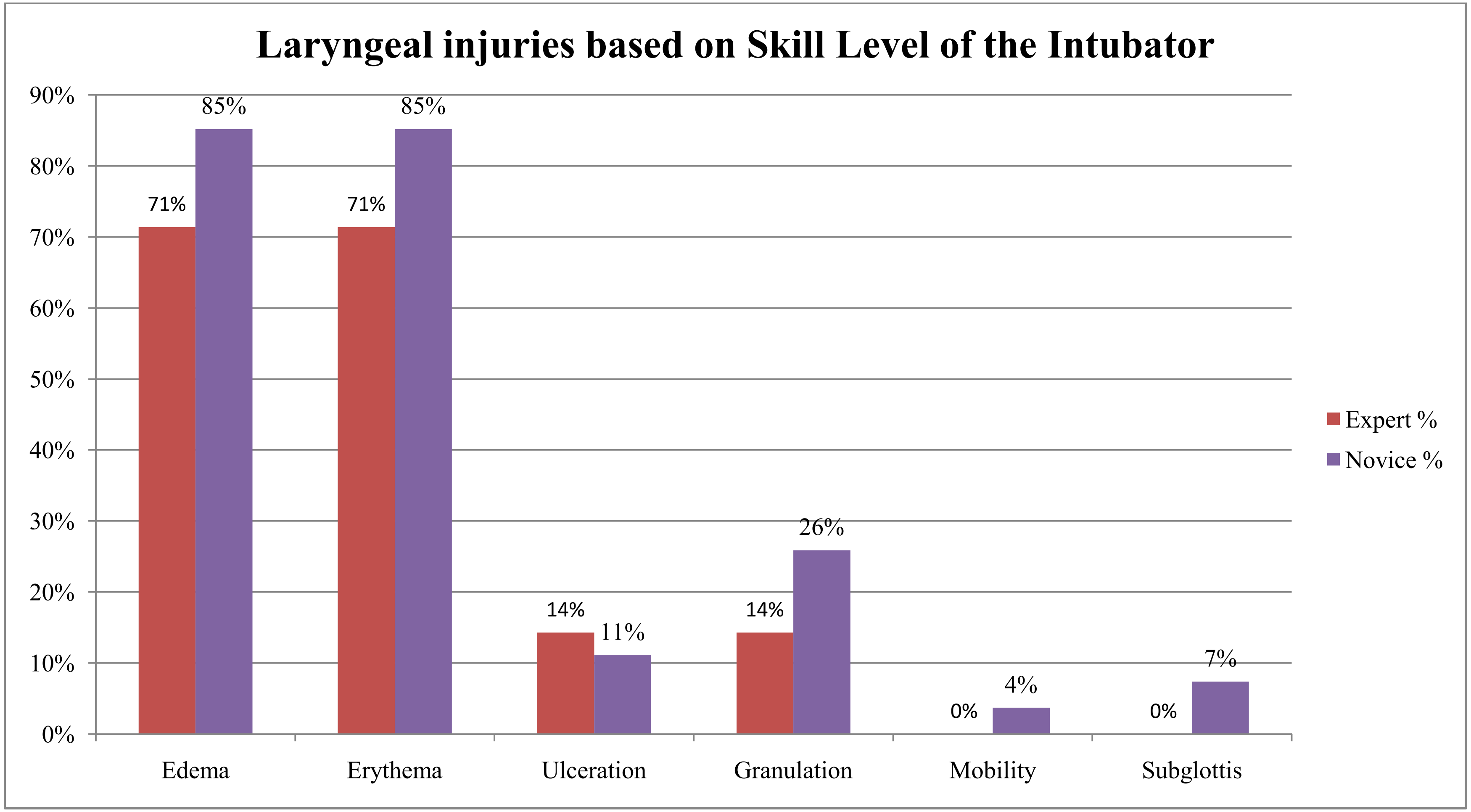
XX. LARYNGEAL INJURIES BASED ON SKILL LEVEL ON INTUBATOR

Table 12: Laryngeal injuries based on skill level of intubator

	Edema	Erythema	Ulceration	Granulation	Mobility	Subglottis
Expert	5	5	1	1	0	0
Expert %	71%	71%	14%	14%	0%	0%
Novice	23	23	3	7	1	2
Novice %	85%	85%	11%	26%	4%	7%

The intubators were broadly classified as 'Novice' and 'Expert' intubators. Novice intubators include the registrars – senior and junior as well as intubators outside the hospital. Anesthetists and Paediatric Intensive care consultants were considered as the Expert intubators. Twenty-seven children were intubated by novice group and seven children were intubated by the expert intubators the Novice group, there was an increase in injuries across the spectrum. Laryngeal oedema and arytenoid erythema was the commonest injury seen in both groups; 85% and 71% respectively (p=0.360). Laryngeal ulceration was seen in 11% in the novice group compared to 14% in the expert group (p=0.622). Laryngeal granulation was seen in 26% and 14% respectively (p=0.465). Vocal fold immobility and subglottic granulations were seen only in novice group.

Figure 35: Laryngeal injuries based on skill level of intubator



XXI. SIGNIFICANCE OF MULTIPLE ATTEMPTS OF INTUBATION.

Only one patient had multiple attempts of intubation. This child developed left vocal cord palsy which recovered in 4 weeks. Repeat endoscopic assessment on follow up was normal.

XXII. CHILDREN REQUIRING INTERVENTION

During the course of the study, six children required intervention (Table 14). Four children required medical intervention and two children surgical intervention. Four children with severe oedema on flexible scopy were treated with systemic steroids for 48 hours and steroid inhalers for 4-6 weeks. The surgical intervention included tracheostomy and debridement of granulations in one child and endoscopic debridement of the subglottic scar tissue in another.

Table 13: Children requiring intervention

No	Patient Details	Intubation details	Findings	Intervention
1	11 year old boy with snake bite	Intubated for 5 days with oversized cuffed tube. Intubated in single attempt by novice intubator.	Laryngeal oedema on initial assessment. On follow up after 3 weeks had subglottic granulations	Medical intervention with Steroids
2	3 year old girl with meningoencephalitis	Intubated for 7 days with appropriate sized uncuffed tube. Intubated in single attempt by novice intubator.	Laryngeal oedema and erythema with subglottic granulations	Medical intervention with steroids
3	8 year old male with intestinal perforation	Intubated for 2 days with appropriate sized uncuffed tube. Intubated in single attempt by novice intubator.	Severe Supraglottic oedema	Medical intervention with steroids
4	1 year old male with dengue fever	Intubated for 7 days with appropriate sized tube. Intubated in single attempt by novice intubator	Post extubation stridor Severe Supraglottic oedema	Medical intervention with steroids
5	2 year old boy, with history of dengue	Intubated for 7 days with appropriate sized uncuffed tube. Intubated in single attempt by novice intubator.	Post extubation stridor Laryngeal oedema with subglottic narrowing.	Surgical intervention Endoscopic scar excision
6	13 year old girl with history of OP poisoning	Intubated for 7 days with appropriate sized cuffed tube. Intubated in single attempt by novice intubator	Post extubation stridor Laryngeal oedema, erythema, and vocal process ulcerations. Glottic and Subglottic granulations	Surgical Intervention Endoscopic debridement with Tracheostomy

Figure 36:

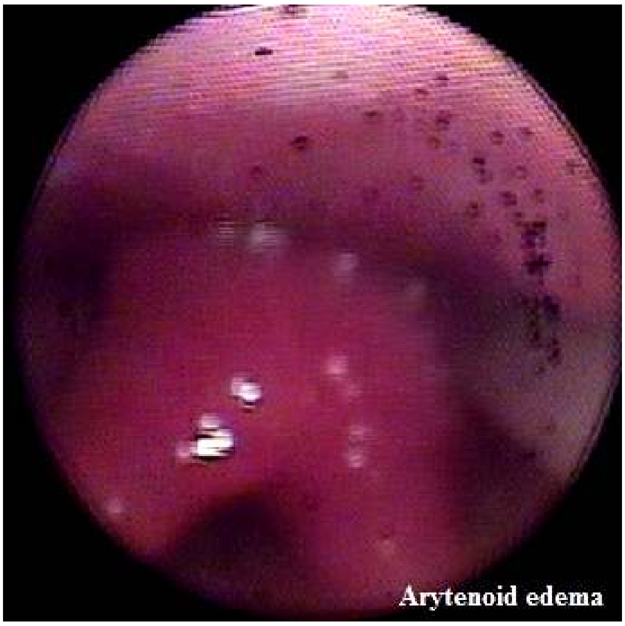


Figure 37:

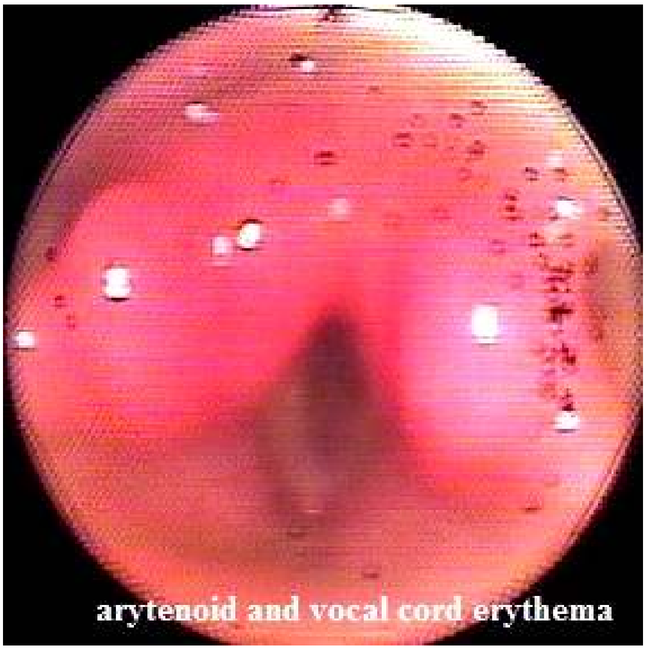


Figure 38:

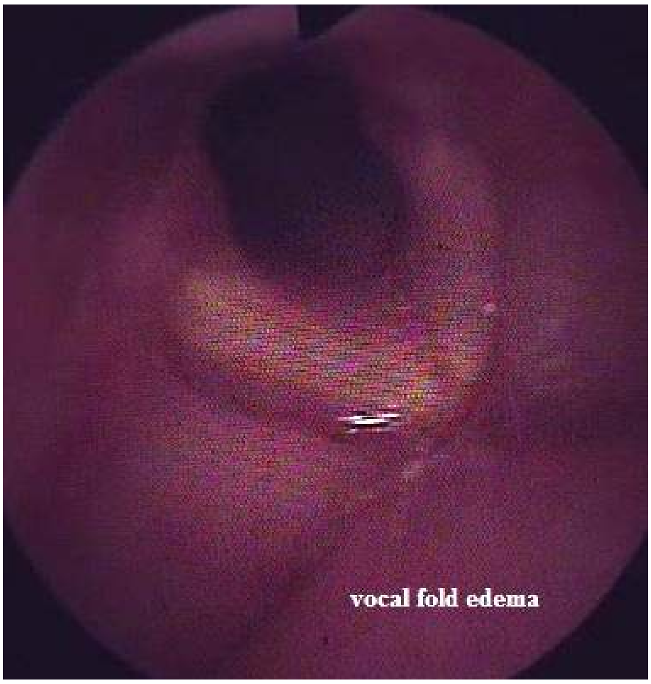


Figure 39:

Figure 40:

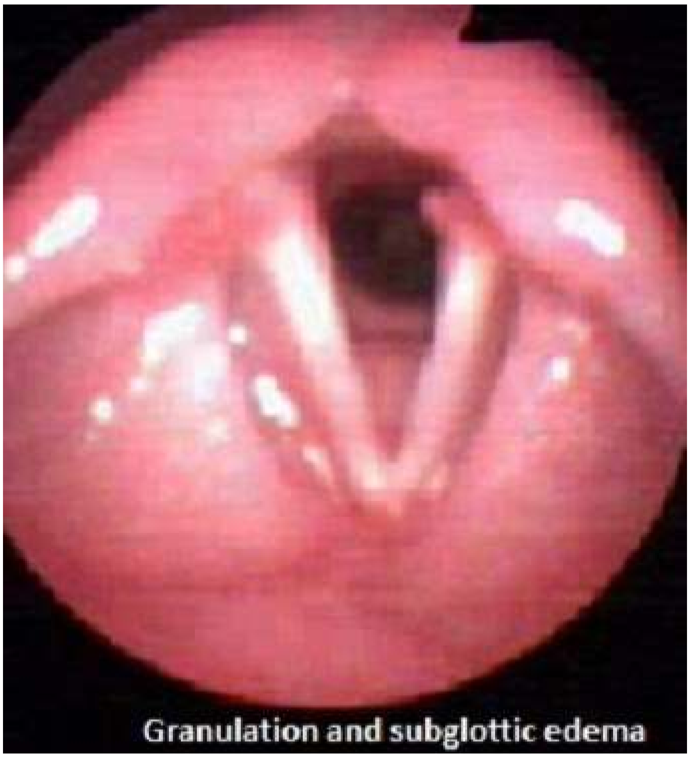


Figure 41:

Figure 42:

DISCUSSION

Post intubation laryngeal injuries have a significant impact on the outcome of the ICU stay. Severe injuries can increase the morbidity and mortality rates with impact on quality of life. Majorities of injuries go unnoticed and heal spontaneously with no or minimal sequelae. However some injuries can cause significant sequelae and have a major impact on the lifestyle of the patient.

Various methods have been proposed to evaluate these injuries and predict outcome of these injuries aimed at improving the outcome. Benjamin et al and Deeb et al suggested evaluation of these injuries by direct laryngoscopy under general anaesthesia, using rigid telescopes and endoscopes. [27, 28] A thorough and complete evaluation of the larynx including subglottis is possible with direct laryngoscopy under general anaesthesia. Also if there is immobility of the vocal cords, differentiation between cord palsy and crico-arytenoid joint subluxation is possible by palpation. Wood et al & Fan et al, however, have preferred bedside examination with the help of flexible scope in awake patients. [47, 48] Smith in a study on 41 children in paediatric intensive care unit noted that flexible laryngoscopy can be performed safely with few minor complications. [50] They also concluded that laryngoscopy can be done easily with good visualization of all regions of the larynx including subglottis. Also, the procedure can be done under local anaesthesia. In our study we screened the children at the bedside using flexible fiberoptic scope.

Colton et al studied patients intubated for at least 48 hours whereas Smith et al studied those intubated for at least 24 hours. [49, 50] Pereira et al retrospectively evaluated all patients who were intubated, irrespective of the duration of intubation.[51] In our study, we included patients who were intubated for at least 48 hours.

There is no consensus on when to evaluate the children after extubation. Colton et al studied the patients within 24 hours of extubation. [49] Laryngeal evaluation was done within 8 hours of extubation by Smith et al. [50] We examined the children within 24 hours of extubation. We felt that all the acute injuries could be safely visualized within 24 hours.

Some form of laryngeal injury is seen in most children who are intubated. All patients (N= 61) in a study by Colton et al had some form of laryngeal injury varying from mild oedema to vocal cord immobility.[49] Smith et al in a study on paediatric population (0-4 yrs) found 93% of children had some degree of injury, of which 51% was mild.[50] In our study 97% had laryngeal injury, 15% being mild. Oedema and erythema were the most common finding in laryngoscopy done immediate post extubation. In our study, laryngeal erythema and oedema were seen in 97 and 94% respectively. Significant oedema was seen in 77%. Vocal process ulceration, granulation and vocal fold immobility were seen in of seven (20%) and one (3%) child respectively. Vocal process granulation was present in ten (29%) and Subglottic narrowing was seen in two patients.

Most studies on laryngeal injuries have been on adult population. [40, 49] Periera et al did a retrospective analysis on infants while Smith et al studied children under five years. [50,51] We included all children but categorized them into two groups; Group 1, children five years or less and group 2, children over five years. Group 1 had sixteen children and group 2 had nineteen children. There was no statistically significant difference between the two groups. Study with larger size is probably needed for demonstrating significant difference between various age groups.

Studies on adult population have shown failure rates of 12-22%, requiring reintubation within 72 hours. [52, 53, 54] In a study on post extubation stridor in paediatric intensive care unit Harel et al identified 32 patients with post extubation stridor and requiring intubation (0.6%). [55] In our study, we had post extubation stridor in three patients. Two of the three children were treated medically. However, one patient needed reintubation (3%).

One of the major causes of post extubation morbidity is need for tracheostomy. Tracheostomy also can be a cause of concern and have a strong negative impact on parents and families. Fear of death from plugged cannula is always present. Experience of changing tracheostomy tube can be frightening. Anxiety about speech development is usual and profound change in lifestyle is warranted. In a nation-wide survey in Switzerland, there was a tracheostomy conversion rate of 1.3%. [56] Smith et al in their study on under fives had two tracheostomies. [50] We did tracheostomy in one patient (3%). The tracheostomy was done prophylactically as the patient had respiratory failure due to neuromuscular weakness. Patient was successfully decannulated in two weeks.

Number of days of ventilation plays a major role in post-extubation outcome of the patient. Periera et al in their retrospective study to identify the factors responsible for failed extubation in neonatal intensive care unit reported that duration of intubation directly affects the incidence of failed extubation and subglottic airway compromise. [51] However, they also noticed that poor pulmonary reserve volume also plays an important role in extubation failure. [51] It was observed that some individuals are able to tolerate this excess pressure to a greater extent while others develop significant injuries even after intubation for few hours or days. Colton et al in their study with intubation range from 2 to 28 days with a mean of 9 days found that the laryngeal injuries were not related to increased duration of intubation.[49] However Santos et al showed a significant correlation between duration of intubation and degree of laryngeal injury(average duration of intubation 9 days).[57,58] In our study, duration of intubation ranged from 2 to 12 days with an average of 4.5 days. There was no significant statistical correlation with laryngeal injuries. However, there appears to be a trend towards subglottis narrowing with prolonged intubation (P value - 0.06). However a study with more number of patients is required to confirm this finding.

Contencin and Narcy in 1993 in a study on newborn infants concluded that the size of endotracheal tube is a significant risk factor for post intubation laryngotracheal stenosis. [59] Pennington's formula (age/4 + 4 for uncuffed and age/4 + 3.5 for cuffed) is used for calculation of the appropriate size of the tube. In our study, 26% of the tubes were oversized. This was needed due to the high ventilator settings. There was no statistical increase in injuries in children intubated with oversized tubes.

In paediatric age group, standard practice is to use uncuffed tube in children less than seven years of age and cuffed tube above this age. [60] Holzki and Khine are strong proponents against the use of cuff tubes in children. [61,62] However, a recent multicentre randomized control trial in 24 European paediatric centres concluded that use of cuffed endotracheal tubes offers a reliably sealed airway with no increase in risk of post extubation stridor. [63]

Experience of the intubator can affect the outcome of the laryngeal injuries. The paediatric larynx is prone for injuries and intubation in children can be a challenge. This is more so when the setting is in the emergency department. Although various authors have commented that the experience of the intubator may be a significant risk factor, there have been no studies which looked into this.[64] In our study we categorized intubators as novice and experienced based on whether they were residents or consultants. We did not find any statistically significant difference between the two groups. This is probably due to the fact that most of the intubations were done by senior residents who might have had a fair bit of experience in tracheal intubations.

Six children required intervention during the course of the study. The first child was a 1- year-old boy with history of snake bite. He was intubated for duration of 5 days with an apparent oversized cuffed endotracheal tube. Laryngoscopy showed laryngeal oedema on initial assessment but subsequently subsided. Subglottic granulations were seen on repeat evaluated after 3 weeks. This child was treated medically with steroid inhalers and followed up.

The second child, a 3-year-old with meningoencephalitis intubated for 7 days with an appropriate sized uncuffed tube. Laryngoscopy showed significant laryngeal oedema and erythema with subglottic granulations. She was treated medically with systemic steroids for 48 hours and steroid inhalers. On re-evaluation after 3 weeks, laryngeal oedema, erythema and granulations had subsided completely.

The third was an 8-year-old male with intestinal perforation intubated for 2 days with an appropriate sized uncuffed tube had severe Supraglottic oedema.

Medical intervention with systemic steroids for 48 hours and steroid inhalers was given and completely recovered by 3 weeks.

The fourth was a 1-year-old with dengue fever, intubated for 7 days with appropriate sized uncuffed tube. He had post extubation stridor and laryngoscopy showed severe Supraglottic oedema. He was treated medically with steroids and subsequently recovered fully.

The fifth child was a 2-year-old boy with dengue fever intubated for 7 days with an appropriate sized uncuffed tube. He had post extubation stridor. Laryngoscopy showed subglottic narrowing. He was treated medically with steroids and followed up. His stridor did not fully recover and had exertional dyspnoea. Repeat scopy at 3 weeks showed grade III subglottic stenosis. He underwent endoscopic debridement of the scar tissue.

The sixth child was a 13-year-old with organophosphate poisoning. She was intubated for 7 days with appropriate sized cuffed tube. She had post extubation stridor. Laryngoscopy showed laryngeal edema, erythema, vocal process ulcerations and glottosubglottic granulations. Surgical intervention was required with endoscopic debridement of granulations. Tracheostomy was done for the ventilator requirements due to neuromuscular involvement due to organophosphate.

STRENGTH AND LIMITATIONS OF THE STUDY

This is a comprehensive study on acute laryngeal injuries in children. We have evaluated the spectrum of injuries associated with intubation using a flexible laryngoscope. We have analyzed the injuries based on the age of the patient, duration of intubation and skill level of the intubator. We have also looked at the size and type of the endotracheal tube used for intubation.

The main limitation of the study is the small sample size. Another limitation is the number of patients who were lost on follow up. A bigger sample probably would be able to find the significance of the various parameters studied.

CONCLUSION

In our study of 34 paediatric patients intubated for more than 48 hours

- 97% had acute laryngeal injury, of which 88% was significant.
- Erythema was the most common form of injury (97%).
- Duration of intubation (mean 4.5 days) shows a trend towards subglottic narrowing (p value-0.06).
- Laryngeal injuries were similar in both cuffed and uncuffed tubes.
- Age, size of the tube and skill level of the intubator did not correlate with the laryngeal injuries.
- 18% required intervention for post-extubation significant oedema
- Three children (10%) had post-extubation stridor; two out of the three (6% of the total) children needed surgical intervention

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APPENDIX-A

PATIENT INFORMATION SHEET

Introduction and purpose of research

Your child has been recruited in this study as he/she had been intubated (tube inside the trachea through mouth/nose) and is in Pediatric Intensive Care Unit for more than 48 hours.

During this process there may be a chance of injury to surrounding structures .This may lead to both short and long term sequelae after extubation. This study will help in detecting such injuries earlier.

If any injury/trauma is seen to be present, an early intervention with standard treatment will be offered to your child to prevent further morbidity.

Test to be done

Following removal of the tube in your child's air passage he/she will undergo examination of that area with the help of a flexible endoscope. This instrument is a thin, soft tube which will be passed through the nose and back of mouth of your child.

Risk/discomfort to the subject

He/she may have mild discomfort during the procedure. Sometimes events like decrease in heart rate and sudden difficulty in breathing may also occur during the procedure, which will need prompt intervention. As this study is an observational study and does not include any trial treatment there is no extra risk for your child due to participation in this study.

Informed consent form for study

Study title: **POST-INTUBATION LARYNGEAL INJURIES IN A PEDIATRIC INTENSIVE CARE UNIT OF TERTIARY HOSPITAL IN INDIA: A FIBREOPTIC ENDOSCOPIC STUDY**

Study number:

*Subject's initials:*______________________*subject's name:*______________________

*Mother's name:*______________________*father's name:*__________________

Date of birth / Age: __________________________*hospital no.-*___________________

Consent given by: *relationship to child:*

i. I confirm that I have read and understood the information sheet dated__________ and have had the opportunity to ask questions.[ ]

ii. I understand that my child's participation in this study is voluntary and that i am free to withdraw my child at any time, without giving any reason, without his/her medical care or legal rights being affected.[ ]

iii. I understand that the sponsor of the study, others working on the sponsor's behalf, the ethics committee and the regulatory authorities will not need any permission to look at his/her health records both in respect of current study and any further research that may be conducted in relation to it, even if he/she withdraws from the study. I agree to this access. However I understand that his/her identity will not be revealed in any information released to the third parties or published.[ ]

iv. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).[ ]

v. I agree to allow my child to take part in above study.[ ]

Signature (or thumb impression) of the subject /legally acceptable representative:

Date: ______ /______ /_____
Signatory's name: ______________

Signature of witness: ___________________
Date: ____________ / __________ / __________
Name of witness: ______________________

APPENDIX-B

Proforma

Name of patient: Hospital number:

Father's /mother's name: Age: Sex:

Weight: Body mass index (BMI):

Primary Diagnosis ___________________________

Indication for intubation: _____________________________

Presence of co morbidities:-

Prematurity	1	2
Larynx: size	small	normal
Larynx abnormal shape	1	2
Abnormal wound healing (keloid formation)	1	2
Septicemia	1	2
Malnutrition	1	2
Congestive cardiac failure	1	2
Diabetes	1	2
Liver disease	1	2
Immunocompormised	1	2
GOR,	1	2
Respiratory arrest	1	2
Cardiac arrest	1	2
Anemia	1	2
Hypotension,	1	2
Bronchopulmonary dysplasia	1	2
Others	_____________________	

(1-YES, 2-NO)

Characteristics of intubation

Intubation 1.Emergency 2.semi-elective 3.planned for surgery

Type of tube 1.cuffed 2.uncuffed

Size of the endotracheal tube (ETT):

Intubator: 1.anesthetist 2.consultant 3. Senior registrar** 4.junior registrar * 5. Other

Use of sedation : 1.YES 2.NO

Use of muscle relaxant drugs: 1.YES 2.NO

Number of attempts for successful intubation: 1. One 2.two 3.multiple
Time taken to intubate 1. 30sec 2. 60sec 3.>60 sec
Difficulty in intubation: 1.yes 2.no
Traumatic intubation : 1.yes 2.no
CPR done: 1.yes 2.no

Cuff pressure**:**
Numbers of days intubated:
No of days ventilated:
Numbers of failed extubation with reintubation:
Intubation followed by tracheotomy: 1.yes 2.no

Nursing
Was patient sedated?
Was suction traumatic and need for repeated suctions?
Nasogastric tube present absent

*Junior registrar- Non pg, Dch
**S enior registrar- M.D. (IIIrd call), ICU fellow

Fiberoptic Laryngoscopic Evaluation (*within 24-48 hours of extubation)***:-**

Arytenoid edema	**0**	**1**	**2**	**3**
Arytenoid erythema	**0**	**1**	**2**	**3**
Interarytenoid edema	**0**	**1**	**2**	**3**
Vocal fold edema	**0**	**1**	**2**	**3**
Vocal fold erythema	**0**	**1**	**2**	**3**
Right vocal process ulceration	**0**	**1**	**2**	**3**
Left vocal process ulceration	**0**	**1**	**2**	**3**
Right vocal process granulation tissue	**0**	**1**	**2**	**3**
Left vocal process granulation tissue	**0**	**1**	**2**	**3**
Right vocal fold immobility	**0**	**1**	**2**	**3**
Left vocal fold immobility	**0**	**1**	**2**	**3**
Subglottic edema/narrowing	**0**	**1**	**2**	**3**

(0 - ***None, 1-Mild, 2-Moderate, 3- Severe*****)**

Complication

Minor

Laryngospasm not requiring ventilation,	1	2
Drop in saturation > 85% - < 92%	1	2
Minor nasal bleeding	1	2

Major

Laryngospasm requiring ventilation	1	2
Desaturation below 85%,	1	2
Bradycardia	1	2

(1-Yes, 2- No)

Fiberoptic Laryngoscopic Evaluation (*after 3-4 weeks)*:-

Arytenoid edema	**0**	**1**	**2**	**3**
Arytenoid erythema	**0**	**1**	**2**	**3**
Interarytenoid edema	**0**	**1**	**2**	**3**
Vocal fold edema	**0**	**1**	**2**	**3**
Vocal fold erythema	**0**	**1**	**2**	**3**
Right vocal process ulceration	**0**	**1**	**2**	**3**
Left vocal process ulceration	**0**	**1**	**2**	**3**
Right vocal process granulation tissue	**0**	**1**	**2**	**3**
Left vocal process granulation tissue	**0**	**1**	**2**	**3**
Right vocal fold immobility	**0**	**1**	**2**	**3**
Left vocal fold immobility	**0**	**1**	**2**	**3**
Subglottic edema/narrowing	**0**	**1**	**2**	**3**

(0 - ***None, 1-Mild, 2-Moderate, 3- Severe)***

Complication

Minor

Laryngospasm not requiring ventilation,	1	2
Drop in saturation > 85% - < 92%	1	2
Minor nasal bleeding	1	2

Major

Laryngospasm requiring ventilation	1	2
Desaturation below 85%,	1	2
Bradycardia	1	2

(1-Yes, 2- No)

APPENDIX-C

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

Dr.B.J.Prashantham, M.A.,M.A.,Dr.Min(Clinical)
Director, Christian Counseling Centre
Editor, Indian Journal of Psychological Counseling
Chairperson, Ethics Committee, IRB

Dr.George Mathew, MS, MD, FCAMS
Chairperson, Research Committee &
Principal

Dr.Gagandeep Kang, MD, Ph.D, FRCPath
Secretary, Research Committee, IRB
Additional Vice Principal(Research)

August 23, 2011

Dr. Bhartendu Bharti
PG Registrar
Department of ENT
Christian Medical College
Vellore 632 004

Sub: **FLUID Research grant Project NEW PROPOSAL:**
Post-intubation laryngeal injuries in a paediatric intensive care unit of tertiary hospital in India: a fibreoptic endoscopic study
Dr. Bhartendu Bharti, PG Registrar, ENT, Dr. Mary Kurien, Dr. Ajoy Mathew Varghese, ENT, Dr. Kala Ebenezer, Paediatric Intensive Care Unit, Dr. J. Ebor Jacob Gnananayagam, Paediatrics, Dr. L. Jeyaseelan, Biostatistics.

Ref: IRB Min. No. 7552 dated 09.08.2011

Dear Dr. Bharti

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled " Post-intubation laryngeal injuries in a paediatric intensive care unit of tertiary hospital in India: a fibreoptic endoscopic study" on August 9, 2011.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Patient Information Sheet and Informed Consent Form (English, Tamil, Hindi and Bengali)
3. Cvs of Drs. Bhartendu Bharti, Mary Kurien, Ajoy Mathew Varghese, Kala Ebenezer, Ebor Jacob Gnananayagam, L. Jeyaseelan.
4. A CD containing document 1 - 3

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

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Dr.George Mathew, MS, MD, FCAMS
Chairperson, Research Committee &
Principal

Dr.Gagandeep Kang, MD, Ph.D, FRCPath
Secretary, Research Committee, IRB
Additional Vice Principal(Research)

The following Institutional Review Board (Ethics Committee) members were present at the meeting held on August 9, 2011 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore - 632002.

Name	Qualification	Designation	Other Affiliations
Dr. B.J.Prashantham	MA (Counseling), MA (Theology), Dr Min(Clinical)	Chairperson(IRB)& Director, Christian Counselling Centre	Non-CMC
Mr. Harikrishnan	BL	Lawyer	Non-CMC
Mrs. S. Pattabiraman	BSc, DSSA	Social Worker, Vellore	Non-CMC
Mrs. Ellen Ebenezer Benjamin (on behalf of Dr. Jayarani Premkumar)	MSc (Nursing), PhD	Nursing Superintendent, CMC	
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M.Phil, BL	Legal Advisor, CMC	
Dr. Jayaprakash Muliyil	BSC, MBBS, MD, MPH, DrPH(Epid), DMHC	Academic Officer, CMC	

We approve the project to be conducted as presented.

The Institutional Ethics Committee / Independent Ethics Committee expects to be informed about the progress of the project, any SAE occurring in the course of the project, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INSTITUTIONAL REVIEW BOARD (IRB)
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Principal

Dr.Gagandeep Kang, MD, Ph.D, FRCPath
Secretary, Research Committee, IRB
Additional Vice Principal(Research)

A sum of ₹ 4700/- (Rupees Four thousand seven hundred only) is sanctioned for 14 months.

Yours sincerely,

Dr. George Mathew
Principal & Chairman (Research Committee)
Institutional Review Board

Dr. George Mathew, MS, MD, FCAMS
Chairperson (Research Committee) &
Principal
Christian Medical College
Vellore - 632 002, Tamil Nadu, India

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Originality GradeMark PeerMark

POST-INTUBATION LARYNGEAL INJURIES IN A PAEDIATRIC

BY BHARTENDU BHARTI 22112252

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INTRODUCTION

In current medical practice, critical care technology and assisted ventilation have grown immensely over the past few decades. Critically ill patients are treated with prolonged assisted ventilation. Intubation is a routine procedure in such patients, and it might take several weeks either to extubate or tracheotomise these patients. Laryngo-tracheal intubation in adults was first done around 1878 by a British surgeon, William McEwen, who used a brass fashioned tube for orotracheal intubation.[1] By 1910's, O'Dwyer, Elsborg, and several others contributed to making it acceptable for induction of anaesthesia. [2 3] It was Bergstorm who first provided prolonged intubation for comatose patients due to head injury or poisoning in 1962.[4] Paediatric intubations, however, were considered unsafe and were not in practice till the 1930's. Subsequent advancements in anaesthesiology in the 1940's made paediatric intubation more acceptable.[5]

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